89446

Access DB# _____

# SEARCH REQUEST FORM

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**Scientific and Technical Information Center**

Requester's Full Name: Jeffrey E. Russel  Examiner #: 62785  Date: 3-19-2003
Art Unit: 1654  Phone Number 308-3975  Serial Number: 10/018,879
Mail Box and Bldg/Room Location: CM1-11D13/CM1-9B07  Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

**********

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

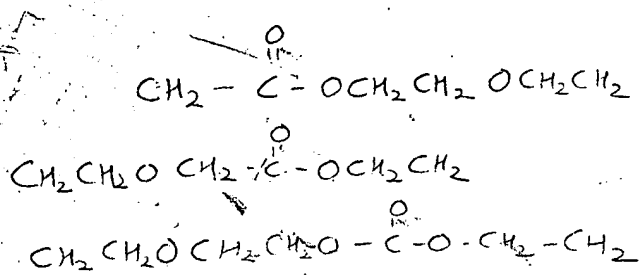
Title of Invention: Amphiphilic Drug-Oligomer Conjugates with Hydrolyzable Lipophile Components

Inventors (please provide full names): N. Ekwuribe, M. Ramaswamy, J. Rajagopalan

Earliest Priority Filing Date: 8-5-2002

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search the following partial structures:



If necessary, keywords are conjugate, protein, polypeptide, peptide, insulin.

Thank you.

JER

Point of Contact:
Mona Smith
Technical Information Specialist
CM1 6A01
Tel: 308-3278

**********

**STAFF USE ONLY**

Searcher: M. Smith
Searcher Phone #: _____
Searcher Location: _____
Date Searcher Picked Up: 3/20/03
Date Completed: 4/1/03
Searcher Prep & Review Time: 60
Clerical Prep Time: _____
Online Time: 75

**Type of Search**

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) X
Bibliographic _____
Litigation _____
Fulltext _____
Patent Family _____
Other _____

**Vendors and cost where applicable**

STN _____
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

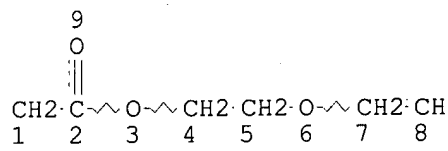
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 15:35:11 ON 10 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 10 Apr 2003 VOL 138 ISS 15
FILE LAST UPDATED: 9 Apr 2003 (20030409/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

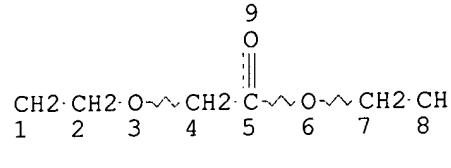
=> d stat que
L1 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L2 ( 6984) SEA FILE=REGISTRY SSS FUL L1
L3 ( 10066) SEA FILE=HCAPLUS L2
L4 89 SEA FILE=HCAPLUS L3 (L) (CONJUG? OR PROTEIN? OR ?PEPTIDE? OR
?INSULIN?)
L5 STR

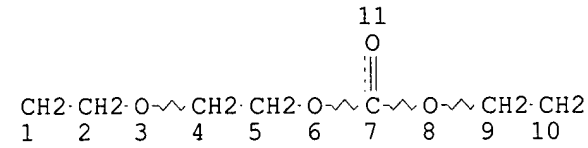



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

Searched by M. Smith

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L6 813 SEA FILE=REGISTRY SSS FUL L5
L7 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L8 406 SEA FILE=REGISTRY SSS FUL L7
L9 570 SEA FILE=HCAPLUS L6
L10 360 SEA FILE=HCAPLUS L8
L12 6543 SEA FILE=REGISTRY INSULIN/BI
L13 155255 SEA FILE=HCAPLUS L12 OR INSULIN
L14 32181 SEA FILE=HCAPLUS CONJUG? (L)(PROTEIN? OR ?PEPTIDE? OR L13)
L15 30 SEA FILE=HCAPLUS L14 AND (L4 OR L9 OR L10)

=> d ibib abs hitrn l15 1-30

L15 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946130 HCAPLUS
DOCUMENT NUMBER: 138:29120
TITLE: Preparation of **peptide** drug-alkylene glycol oligomer **conjugates**
INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002098446 | A1 | 20021212 | WO 2002-US17567 | 20020604 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | |
|---|---|---|---|---|---|
| BR 2001006401 | A | 20030211 | BR 2001-6401 | | 20011011 |
| JP 2003104913 | A2 | 20030409 | JP 2001-317307 | | 20011015 |

PRIORITY APPLN. INFO.: US 2001-873797 A 20010604
OTHER SOURCE(S): MARPAT 138:29120

AB A non-polydispersed mixt. of **conjugates** in which each **conjugate** in the mixt. comprises a **peptide** drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar **conjugates**. The mixt. may be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar **conjugates**. The mixt. may result in less inter-subject variability than polydispersed mixts. of similar **conjugates**. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human growth hormone (Saizen) was allowed to react with the NHS ester to give the **conjugate**.

IT **62304-85-2P 70802-40-3P 477775-74-9P 477775-75-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in alkylene glycol derivs. prepn.; prepn. of **peptide** drug-alkylene glycol oligomer **conjugates**)

IT **259228-98-3P 477775-76-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **peptide** drug-alkylene glycol oligomer **conjugates**)

IT **8049-62-5DP**, Zinc **insulin, conjugates** with alkylene glycols **9004-10-8DP, Insulin, conjugates** with alkylene glycols **11061-68-0DP**, Human **insulin, conjugates** with alkylene glycols **59112-80-0DP**, C-**Peptide, conjugates** with alkylene glycols **106602-62-4DP**, Amylin, **conjugates** with alkylene glycols **259228-98-3DP, peptide** drug **conjugates 477775-76-1DP, peptide** drug **conjugates**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **peptide** drug-alkylene glycol oligomer **conjugates**)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946037 HCAPLUS
DOCUMENT NUMBER: 138:16621
TITLE: Preparation of **insulin**-alkylene glycol oligomer **conjugates**
INVENTOR(S): Ekwuribe, Nnochiri N.; Price, Christopher H.; Ansari, Aslam M.; Odenbaugh, Amy L.; Radhakrishnan, Balasingam
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002098232 | A1 | 20021212 | WO 2002-US17574 | 20020604 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 2003027748 | A1 | 20030206 | US 2001-873899 | 20010604 |

PRIORITY APPLN. INFO.: US 2001-873899 A 20010604
OTHER SOURCE(S): MARPAT 138:16621

AB A mixt. of **conjugates** in which each **conjugate** in the mixt. comprises an **insulin** drug coupled to an oligomer that includes a polyalkylene glycol moiety is disclosed. The mixt. may exhibit higher in vivo activity than a polydispersed mixt. of similar **conjugates**. The mixt. may also be more effective at surviving an in vitro model of intestinal digestion than polydispersed mixts. of similar **conjugates**. The mixt. may also result in less inter-subject variability than polydispersed mixts. of similar **conjugates**. Thus, non-polydispersed hexaethylene glycol was treated with phosgene soln., followed by treatment with N-hydroxysuccinimide (NHS) to give give the NHS ester. Human **insulin** was dissolved in DMSO and allowed to react with the NHS ester to give the **conjugate**.

IT **62304-85-2P 70802-40-3P 477775-74-9P**
**477775-75-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in alkylene glycol derivs. prepn.; prepn. of **insulin**-alkylene glycol oligomer **conjugates**)

IT **8049-62-5DP**, Zinc **Insulin**, alkylene glycol oligomer **conjugates** **9004-10-8DP**, **Insulin**, alkylene glycol oligomer **conjugates** **11061-68-0DP**, Human **insulin**, alkylene glycol oligomer **conjugates**
**259228-98-3DP**, **insulin conjugates**
**477775-76-1DP**, **insulin conjugates**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of **insulin**-alkylene glycol oligomer **conjugates**)

IT **259228-98-3P 477775-76-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of **insulin**-alkylene glycol oligomer **conjugates**)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:700064 HCAPLUS
DOCUMENT NUMBER: 138:122793
TITLE: A new and efficient method for synthesis of 5'-conjugates of oligonucleotides through amide-bond formation on solid phase
AUTHOR(S): Kachalova, Anna V.; Stetsenko, Dmitry A.; Romanova, Elena A.; Tashlitsky, Vadim N.; Gait, Michael J.; Oretskaya, Tatiana S.
CORPORATE SOURCE: Chemistry Department and A. N. Belozersky Institute of Physico-Chemical Biology, M. V. Lomonosov Moscow State University, Moscow, 119992, Russia
SOURCE: Helvetica Chimica Acta (2002), 85(8), 2409-2416
CODEN: HCACAV; ISSN: 0018-019X
PUBLISHER: Verlag Helvetica Chimica Acta
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:122793

AB An efficient method for synthesis of oligonucleotide 5'-**conjugates** through amide-bond formation on solid phase is described. Protected oligonucleotides contg. a 5'-carboxylic acid function were obtained by use of a novel non-nucleosidic phosphoramidite building block, where the carboxylic acid moiety was protected by a 2-chlorotrityl group. The protecting group is stable to the phosphoramidite coupling conditions used in solid-phase oligonucleotide assembly, but is easily deprotected by mild acidic treatment. The protecting group may be removed also by ammonolysis. 5'-Carboxylate-modified oligonucleotides were efficiently on solid support under normal **peptide**-coupling conditions to various amines or to the N-termini of small **peptides** to yield products of high purity. The method is well-suited in principle for the synthesis of **peptide**-oligonucleotide **conjugates** contg. an amide linkage between the 5'-end of an oligonucleotide and the N-terminus of a **peptide**.

IT **199869-48-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid phase synthesis of 5'-**conjugates** of oligonucleotides through amide-bond formation)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:324975 HCAPLUS
DOCUMENT NUMBER: 137:90504
TITLE: Carbohydrate arrays for the evaluation of protein binding and enzymatic modification
AUTHOR(S): Houseman, Benjamin T.; Mrksich, Milan
CORPORATE SOURCE: The Institute for Biophysical Dynamics, Deparmtent of Chemistry, The University of Chicago, Chicago, IL, 60637, USA
SOURCE: Chemistry & Biology (2002), 9(4), 443-454
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This paper reports a chem. strategy for prepg. carbohydrate arrays and utilizes these arrays for the characterization of carbohydrate-**protein** interactions. Carbohydrate chips were prepd. by the Diels-Alder-mediated immobilization of carbohydrate-cyclopentadiene **conjugates** to self-assembled monolayers that present benzoquinone and penta(ethylene glycol) groups. Surface plasmon resonance spectroscopy

showed that lectins bound specifically to immobilized carbohydrates and that the glycol groups prevented nonspecific **protein** adsorption. Carbohydrate arrays presenting ten monosaccharides were then evaluated by profiling the binding specificities of several lectins. These arrays were also used to det. the inhibitory concns. of sol. carbohydrates for lectins and to characterize the substrate specificity of .beta.-1,4-galactosyltransferase. Finally, a strategy for prepg. arrays with carbohydrates generated on solid phase is shown. This surface engineering strategy will permit the prepn. and evaluation of carbohydrate arrays that present diverse and complex structures.

IT **154773-34-9P 441775-29-7P 441775-30-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(carbohydrate arrays for evaluation of protein binding and enzymic modification)

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:409049 HCAPLUS
DOCUMENT NUMBER: 135:167010
TITLE: A Convenient Solid-Phase Method for Synthesis of 3'-Conjugates of Oligonucleotides
AUTHOR(S): Stetsenko, Dmitry A.; Gait, Michael J.
CORPORATE SOURCE: Laboratory of Molecular Biology, Medical Research Council, Cambridge, CB2 2QH, UK
SOURCE: Bioconjugate Chemistry (2001), 12(4), 576-586
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:167010

AB We present a new procedure for the prepn. of 3'-**conjugates** of oligonucleotides through solid-phase synthesis. A suitable universal solid support was readily prepd. using a series of **peptide**-like coupling reactions to incorporate first a spacer and then an L-homoserine branching unit. The N-.alpha.-position of the homoserine carries an Fmoc protecting group that is removed by treatment with piperidine to liberate an amino group suitable for attachment of the **conjugate** (e.g., small org. mol., fluorescent group, cholesterol, biotin, amino acid, etc.) or for assembly of a short **peptide**. The side-chain hydroxyl group of the homoserine carries a trityl protecting group. After TFA deprotection, the hydroxyl group acts as the site for oligonucleotide assembly. An addnl. spacer, such as aminohexanoyl, may be incorporated easily between the **conjugate** mol. and the oligonucleotide. A no. of examples of synthesis of 3'-**conjugates** of oligonucleotides and their analogs are described that involve std. automated oligonucleotide assembly and use of com. available materials. The linkage between oligonucleotide and 3'-**conjugate** is chirally pure and is stable to conventional ammonia treatment used for oligonucleotide deprotection and release from the solid support. The homoserine-functionalized solid support system represents a simple and universal route to 3'-**conjugates** of oligonucleotides and their derivs.

IT **352535-99-0P 352536-02-8DP**, controlled pore glass support **352536-04-0DP**, controlled pore glass support **352536-10-8DP**, controlled pore glass support **352536-12-0DP**, controlled pore glass support **352536-14-2DP**, controlled pore glass support **353241-41-5DP**, controlled pore glass support

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(solid phase synthesis of **conjugates** of **peptide** -contg. oligonucleotides)
REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:409048 HCAPLUS
DOCUMENT NUMBER: 135:157549
TITLE: Studies on Protein-Liposome Coupling Using Novel Thiol-Reactive Coupling Lipids: Influence of Spacer Length and Polarity
AUTHOR(S): Fleiner, Michael; Benzinger, Petra; Fichert, Thomas; Massing, Ulrich
CORPORATE SOURCE: Department of Clinical Research, Tumor Biology Center, Freiburg, D-79106, Germany
SOURCE: Bioconjugate Chemistry (2001), 12(4), 470-475
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To optimize the prepn. of immunoliposomes, we investigated the coupling of thiolated IgG and BSA to liposomes using a novel group of coupling lipids. All lipids consist of cholesterol as membrane anchor and a thiol-reactive maleimide headgroup, linked by a spacer that differs in length and polarity (ethylene glycol, tetraethylene glycol, PEG 400, PEG 1000, dodecyl). In addn., lipids differ in the electrophilicity of the maleimide group (p- or m-maleimidobenzoic ester). In the case of BSA, coupling efficiency strongly depended on the electrophilicity of the maleimide group as well as on the spacer polarity: the less electrophilic meta constitution seems to be an advantage over the p-maleimidobenzoic ester, resulting in higher coupling efficiency. Polar spacers (tetraethylene glycol, 46%) achieved a higher coupling efficiency than a nonpolar spacer with approx. the same length (dodecyl, 15%). When liposomes contg. coupling lipids with the spacers tetraethylene glycol, PEG 400, and PEG 1000 were linked to BSA, coupling efficiencies were in a medium range and similar (41-46%) but were lower for the short ethylene glycol spacer (30%). In contrast, for IgG coupling efficiencies correlated with increasing spacer length. Best results were obtained using coupling lipids with a long polar spacer (PEG 1000) (65%), whereas a coupling lipid bearing a short spacer (ethylene glycol) resulted in a low coupling efficiency of 12%.
IT **204652-44-8P 204652-45-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(spacer length and polarity effect on **protein**-liposome coupling using thiol-reactive coupling lipids)
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:255941 HCAPLUS
DOCUMENT NUMBER: 134:266736
TITLE: Soluble, degradable poly(ethylene glycol) derivatives for controllable release of bound molecules into solution
INVENTOR(S): Harris, J. Milton
PATENT ASSIGNEE(S): Shearwater Corporation, USA

SOURCE: U.S., 13 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 6214966 | B1 | 20010410 | US 1997-937846 | 19970925 |
| US 2001021763 | A1 | 20010913 | US 2001-824297 | 20010402 |
| US 6515100 | B2 | 20030204 | | |

PRIORITY APPLN. INFO.: US 1996-26716P P 19960926
US 1997-937846 A3 19970925

AB PEG and related polymer derivs. having weak, hydrolytically unstable linkages near the reactive end of the polymer are provided for **conjugation** to drugs, including **proteins**, enzymes, small mols., and others. These derivs. provide a sufficient circulation period for a drug-PEG **conjugate** and then for hydrolytic breakdown of the **conjugate** and release of the bound mol. In some cases, drugs that previously had reduced activity when permanently coupled to PEG can have therapeutically suitable activity when coupled to a degradable PEG in accordance with the invention. The PEG of the invention can be used to impart water soly., size, slow rate of kidney clearance, and reduced immunogenicity to the **conjugate**. Controlled hydrolytic release of the bound mol. in the aq. environment can then enhance the drug delivery system. Polyethylene glycol Me 2-(2-pyridyldithio)ethoxycarbonylmethyl ether was prepd. and the hydrolytic half-life of the ester linkage detd.

IT **331968-66-2P 331968-70-8P 331968-74-2P**
**331968-77-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(sol., degradable polyethylene glycol derivs. for controllable release of bound mols. into soln.)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:911065 HCAPLUS
DOCUMENT NUMBER: 134:76386
TITLE: Amphiphilic drug-oligomer conjugates with hydrolyzable lipophile components and methods for making and using the same
INVENTOR(S): Ekwuribe, Nnochiri; Ramaswamy, Muthukumar; Rajagopalan, Jayanthi
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000078302 | A1 | 20001228 | WO 2000-US16879 | 20000619 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| US 6309633 | B1 | 20011030 | US 1999-336548 | 19990619 |
| BR 2000011772 | A | 20020402 | BR 2000-11772 | 20000619 |
| EP 1196157 | A1 | 20020417 | EP 2000-942956 | 20000619 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2003502364 | T2 | 20030121 | JP 2001-504366 | 20000619 |
| NO 2001006143 | A | 20020218 | NO 2001-6143 | 20011217 |

PRIORITY APPLN. INFO.: US 1999-336548 A 19990619
WO 2000-US16879 W 20000619

AB The present invention relates generally to hydrolyzable drug-oligomer **conjugates**, pharmaceutical compns. comprising such **conjugates**, and to methods for making and using such **conjugates** and pharmaceutical compns. For example, a **conjugate** of **insulin**, PEG, and oleic acid was prepd. and can be orally administered.

IT **59392-49-3**, Gastric inhibitory **peptide**
**61912-98-9**, **Insulin**-like growth factor
**67763-96-6**, **Insulin**-like growth factor I
**67763-97-7**, **Insulin**-like growth factor II
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amphiphilic drug-oligomer **conjugates** with hydrolyzable lipophile components)

IT **9004-10-8**, **Insulin**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(amphiphilic drug-oligomer **conjugates** with hydrolyzable lipophile components)

IT **10233-14-4P**, Triethylene glycol oleate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amphiphilic drug-oligomer **conjugates** with hydrolyzable lipophile components)

IT **9004-10-8DP**, **Insulin**, **conjugates** with PEG derivs., biological studies **10233-14-4DP**, Triethylene glycol oleate, **conjugates** with **insulin 28397-10-6DP**, Octanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester, **conjugates** with **insulin 62304-85-2DP**, Hexadecanoic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester, **conjugates** with **insulin**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amphiphilic drug-oligomer **conjugates** with hydrolyzable lipophile components)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:788342 HCAPLUS
DOCUMENT NUMBER: 134:136545
TITLE: Design of folic acid-conjugated nanoparticles for drug targeting
AUTHOR(S): Stella, Barbara; Arpicco, Silvia; Peracchia, Maria

Teresa; Desmaele, Didier; Hoebeke, Johan; Renoir, Michel; D'Angelo, Jean; Cattel, Luigi; Couvreur, Patrick
CORPORATE SOURCE: Universite Paris-Sud XI, Physico-Chimie-Pharmacotechnie-Biopharmacie, UMR CNRS 8612-5, Chatenay-Malabry, 92296, Fr.
SOURCE: Journal of Pharmaceutical Sciences (2000), 89(11), 1452-1464
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The new concept developed in this study is the design of poly(ethylene glycol) (PEG)-coated biodegradable nanoparticles coupled to folic acid to target the folate-binding **protein**; this mol. is the sol. form of the folate receptor that is overexpressed on the surface of many tumoral cells. For this purpose, a novel copolymer, the poly[aminopoly(ethylene glycol)cyanoacrylate-co-hexadecyl cyanoacrylate] [poly(H2NPEGCA-co-HDCA)] was synthesized and characterized. Then nanoparticles were prepd. by nanopptn. of the obtained copolymer, and their size, zeta potential, and surface hydrophobicity were investigated. Nanoparticles were then **conjugated** to the activated folic acid via PEG terminal amino groups and purified from unreacted products. Finally, the specific interaction between the **conjugate** folate-nanoparticles and the folate-binding **protein** was evaluated by surface plasmon resonance. This anal. confirmed a specific binding of the folate-nanoparticles to the folate-binding **protein**. This interaction did not occur with nonconjugated nanoparticles used as control. Thus, folate-linked nanoparticles represent a potential new drug carrier for tumor cell-selective targeting.

IT **321905-00-4DP**, deprotected
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(design of folic acid-**conjugated** nanoparticles for drug targeting)

IT **321904-99-8P 321905-00-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design of folic acid-**conjugated** nanoparticles for drug targeting)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:755211 HCAPLUS
DOCUMENT NUMBER: 133:340208
TITLE: Novel compositions useful for delivering anti-inflammatory agents into a cell
INVENTOR(S): Unger, Evan C.; McCreery, Thomas; Sadewasser, David A.
PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| EP 1046394 | A2 | 20001025 | EP 2000-303249 | 20000418 |
| EP 1046394 | A3 | 20011010 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1999-294623 A 19990419

AB The present invention is directed, inter alia, to compns. and their use for delivering compds. into a cell. In a preferred embodiment, the compns. comprise, in combination with the compd. to be delivered, an org. halide, a targeting ligand, and a nuclear localization sequence, optionally in the presence of a carrier. Ultrasound may be applied, if desired. The compns. are particularly suitable for the treatment of inflammatory diseases.

IT **303096-39-1P 303096-53-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**peptide** compns. useful for delivering anti-inflammatory agents into a cell)

IT **303096-30-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**peptide** compns. useful for delivering anti-inflammatory agents into a cell)

L15 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:133428 HCAPLUS
DOCUMENT NUMBER: 132:185416
TITLE: Blood-brain barrier therapeutics
INVENTOR(S): Ekwuribe, Nnochiri N.; Radhakrishnan, Balasingam; Price, Christopher H.; Anderson, Wesley R., Jr.; Ausari, Aslam M.
PATENT ASSIGNEE(S): Protein Delivery, Inc., USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000009073 | A2 | 20000224 | WO 1999-US18248 | 19990812 |
| WO 2000009073 | A3 | 20000629 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2340418 | AA | 20000224 | CA 1999-2340418 | 19990812 |
| AU 9956726 | A1 | 20000306 | AU 1999-56726 | 19990812 |
| EP 1105142 | A2 | 20010613 | EP 1999-943676 | 19990812 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

| | | | | |
|---|---|---|---|---|
| BR 9914280 | A | 20011113 | BR 1999-14280 | 19990812 |
| JP 2002522463 | T2 | 20020723 | JP 2000-564577 | 19990812 |

PRIORITY APPLN. INFO.: US 1998-134803 A 19980814

WO 1999-US18248 W 19990812

AB The present invention relates to amphiphilic drug-oligomer **conjugates** capable of traversing the blood-brain barrier and to methods of making and using such **conjugates**. Amphiphilic drug-oligomer **conjugates** comprise a therapeutic compd. **conjugated** to an oligomer, wherein the oligomer comprises a lipophilic moiety coupled to a hydrophilic moiety. The **conjugates** of the invention further comprise therapeutic agents such as **proteins, peptides,** nucleosides, nucleotides, antiviral agents, antineoplastic agents, antibiotics, etc., and prodrugs, precursors, derivs. and intermediates thereof, chem. coupled to amphiphilic oligomers. One example **conjugate** prepd. was Met-enkephalin with a succinimidyl triethylene glycol monohexadecyl ester deriv.

IT **9004-10-8DP, Insulin, conjugates** with polyoxyalkylene deriv., biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(blood-brain barrier therapeutics comprising drug-oligomer **conjugates**)

IT **62304-85-2P,** Triethylene glycol monohexadecanoate **259228-98-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(blood-brain barrier therapeutics comprising drug-oligomer **conjugates**)

IT **62304-85-2DP, conjugates** with enkephalin **259229-01-1DP, conjugates** with enkephalin **259229-02-2DP, conjugates** with enkephalin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(blood-brain barrier therapeutics comprising drug-oligomer **conjugates**)

IT **259229-07-7 259229-08-8**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood-brain barrier therapeutics comprising drug-oligomer **conjugates**)

L15 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:81382 HCAPLUS
DOCUMENT NUMBER: 132:251326
TITLE: Synthesis of end-labeled multivalent ligands for exploring cell-surface-receptor-ligand interactions
AUTHOR(S): Gordon, Eva J.; Gestwicki, Jason E.; Strong, Laura E.; Kiessling, Laura L.
CORPORATE SOURCE: Departments of Chemistry and Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Chemistry & Biology (2000), 7(1), 9-16
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:251326

AB Background: Ring-opening metathesis polymn. (ROMP) is a powerful synthetic method for generating unique materials. The functional group tolerance of ruthenium ROMP initiators allows the synthesis of a wide range of biol. active polymers. We generated multivalent ligands that inhibit cell surface L-selectin, a **protein** that mediates lymphocyte homing

and leukocyte recruitment in inflammation. We hypothesized that these ligands function through specific, multivalent binding to L-selectin. To examine this and to develop a general method for synthesizing multivalent materials with end-labels, we investigated functionalized enol ethers as capping agents in ruthenium-initiated ROMP. Results: We synthesized a bifunctional mol. that introduces a unique end group by terminating ruthenium-initiated ROMP reactions. This agent contains an enol ether at one end and a masked carboxylic acid at the other. We **conjugated** a fluorescein deriv. to an end-capped neoglycopolymer that had previously been shown to inhibit L-selectin function. We used fluorescence microscopy to visualize neoglycopolymer binding to cells displaying L-selectin. Our results suggest that the neoglycopolymers bind specifically to cell surface L-selectin through multivalent interactions. Conclusions: Ruthenium-initiated ROMP can be used to generate biol. active, multivalent ligands terminated with a latent functional group. The functionalized polymers can be labeled with a variety of mol. tags, including fluorescent mols., biotin, lipids or antibodies. The ability to **conjugate** reporter groups to ROMP polymers using this strategy has broad applications in the material and biol. sciences.

IT **262857-77-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of end-labeled multivalent ligands fluorescein neoglycopolymer for exploring cell-surface-receptor-ligand interactions)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:484864 HCAPLUS
DOCUMENT NUMBER: 131:272145
TITLE: Synthesis of Novel GABA Uptake Inhibitors. 3. Diaryloxime and Diarylvinyl Ether Derivatives of Nipecotic Acid and Guvacine as Anticonvulsant Agents
AUTHOR(S): Knutsen, Lars J. S.; Andersen, Knud Erik; Lau, Jesper; Lundt, Behrend F.; Henry, Rodger F.; Morton, Howard E.; Nrum, Lars; Petersen, Hans; Stephensen, Henrik; Suzdak, Peter D.; Swedberg, Michael D. B.; Thomsen, Christian; Sorensen, Per O.
CORPORATE SOURCE: Health Care Discovery and Development, Novo Nordisk A/S, Malov, DK-2760, Den.
SOURCE: Journal of Medicinal Chemistry (1999), 42(18), 3447-3462
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB (3R)-1-[4,4-bis(3-methyl-2-thienyl)-3-butenyl]-3-piperidinecarboxylic acid (tiagabine, Gabitril) is a potent and selective .gamma.-aminobutyric acid (GABA) uptake inhibitor with proven anticonvulsant efficacy in humans. This drug, which has a unique mechanism of action among marketed anticonvulsant agents, has been launched for add-on treatment of partial seizures with or without secondary generalization in patients >12 yr of age. Using this new agent as a benchmark, we have designed two series of novel GABA uptake inhibitors of remarkable potency, using a putative new model of ligand interaction at the GABA transporter type 1 (GAT-1) uptake site. This model involves the postulated interaction of an electroneg. region in the GABA uptake inhibitor with a pos. charged domain in the **protein** structure of the GAT-1 site. These two novel series of

anticonvulsant agents contain diaryloxime or diarylvinyl ether functionalities linked to cyclic amino acid moieties and were derived utilizing the new model, via a series of design steps from the known 4,4-diarylbutenyl GABA uptake inhibitors. The new compds. are potent inhibitors of [3H]-GABA uptake in rat brain synaptosomes in vitro, and their antiepileptic potential was demonstrated in vivo by their ability to protect against seizures induced by the benzodiazepine receptor inverse agonist Me 4-ethyl-6,7-dimethoxy-.beta.-carboline-3-carboxylate (DMCM) in mice. From structure-activity studies of these new GABA uptake inhibitors, we have shown that insertion of an ether oxygen in **conjugation** with the double bond in tiagabine (Ki = 67 nM) improves in vitro potency by 5-fold to 14 nM.

IT **131029-43-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of diaryloxime and diarylvinyl ether derivs. of nipecotic acid and guvacine as anticonvulsant agents)

REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:460345 HCAPLUS
DOCUMENT NUMBER: 131:88341
TITLE: Polyamide oligomers and their use in drug delivery via liposomes
INVENTOR(S): Ansell, Steven Michial
PATENT ASSIGNEE(S): Inex Pharmaceuticals Corporation, Can.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9933493 | A1 | 19990708 | WO 1998-CA1185 | 19981222 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2315695 | AA | 19990708 | CA 1998-2315695 | 19981222 |
| AU 9917460 | A1 | 19990719 | AU 1999-17460 | 19981222 |
| AU 751434 | B2 | 20020815 | | |
| EP 1041976 | A1 | 20001011 | EP 1998-962158 | 19981222 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6320017 | B1 | 20011120 | US 1998-218988 | 19981222 |
| JP 2001527052 | T2 | 20011225 | JP 2000-526243 | 19981222 |
| US 2002026027 | A1 | 20020228 | US 2001-944282 | 20010830 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1997-113658P | P | 19971223 |
| US 1998-73852P | P | 19980202 |
| US 1997-996783 | A1 | 19971223 |
| US 1998-218988 | A3 | 19981222 |
| WO 1998-CA1185 | W | 19981222 |

AB Polyamide oligomers which can be **conjugated** to lipids, nucleic acids, **peptides**, **proteins**, etc., to form liposomes, virusomes, micelles, etc., optionally contg. drugs or biol. agents, have the structure R[NR1(CH2CH2O)m(CH2)pCO(NHCHR2CO)q]nR3 [R = H, alkyl, acyl; each R1 = H, alkyl; or terminal NRR1 = N3; R2 = H, (un)substituted alkyl or aryl, amino acid side chain residue; R3 = H, halogen, OH, SH, alkoxy, NHNH2, NR4R5; R4, R5 = H, alkyl; m = 2-6; n = 4-80; p = 1-4; q = 0, 1]. Thus, tetraethylene glycol was monoetherified with dihydropyran, the resulting acetal etherified with BrCH2CO2Et and deprotected, and the terminal OH replaced by N3 to give N3(CH2CH2O)4CH2CO2Et, part of which was reduced to the NH2 deriv. and part of which was hydrolyzed to the acid, after which the 2 products were condensed by use of dicyclohexylcarbodiimide to give N3(CH2CH2O)4CH2CONH(CH2CH2O)4CH2CO2Et. Two repetitions of this coupling procedure gave N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7OEt, which was sapond. and converted to N3(CH2CH2O)4CH2CO[NH(CH2CH2O)4CH2CO]7NHCH2CH2OP(O)(OH)OCH2CH[O2C(CH2)16Me]CH2O2C(CH2)16Me.

IT **154773-34-9P 229645-50-5P**, Ethyl 14-amino-3,6,9,12-tetraoxatetradecanoate **229645-52-7P 229645-54-9P 229645-56-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(polyamide oligomers for use in drug delivery via liposomes)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:317199 HCAPLUS
DOCUMENT NUMBER: 130:357165
TITLE: Delivery of polyethylene glycol-conjugated molecules from degradable hydrogels
INVENTOR(S): Harris, J. Milton
PATENT ASSIGNEE(S): Shearwater Polymers, Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9922770 | A1 | 19990514 | WO 1998-US918 | 19980123 |
| W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6258351 | B1 | 20010710 | US 1997-964972 | 19971105 |
| CA 2304976 | AA | 19990514 | CA 1998-2304976 | 19980123 |
| AU 9860291 | A1 | 19990524 | AU 1998-60291 | 19980123 |
| AU 752747 | B2 | 20020926 | | |
| EP 1028753 | A1 | 20000823 | EP 1998-903543 | 19980123 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

| | | | | | |
|---|---|---|---|---|---|
| JP 2001523637 | T2 | 20011127 | JP 2000-518700 | | 19980123 |
| US 6432397 | B1 | 20020813 | US 1999-426289 | | 19991025 |
| US 2002032281 | A1 | 20020314 | US 2001-824265 | | 20010402 |
| PRIORITY APPLN. INFO.: | | | US 1997-964972 | A | 19971105 |
| | | | US 1996-30453P | P | 19961106 |
| | | | WO 1998-US918 | W | 19980123 |
| | | | US 1999-426289 | A3 | 19991025 |

AB A degradable, chem. crosslinked PEG hydrogel is described for controlled release, by hydrolysis, of **conjugates** of substantially nonpeptidic polymers such as PEG with biol. active mols. For example, PEG and **protein conjugates** can be released in vivo from the hydrogels for therapeutic application. The crosslinked hydrogels are formed by reaction of (1) active branched derivs. of PEG with (2) amino groups on the biol. active mol. and with (3) amino groups on other PEG mols. or other nonpeptidic polymers contg. hydrolyzable linkages such as carboxylate ester, phosphate ester, acetal, imine, ortho ester, **peptide**, anhydride, ketal, or oligonucleotide linkages in the PEG backbone. The hydrolytic breakdown rate can be controlled by variation of the hydrolyzable linkage and of the degree of bonding (branching) of the branched PEG. Thus, PhCH2(OCH2CH2)nOCH2CO2H was converted to the acid chloride with SOCl2 and condensed with PhCH2(OCH2CH2)nOH; the resulting PhCH2(OCH2CH2)nOCH2CO2(CH2CH2O)nCH2Ph was subjected to hydrogenolysis over Pd/C and condensed with disuccinimidyl carbonate to form NHS-O2C(OCH2CH2)nOCH2CO2(CH2CH2O)nCO2-NHS (NHS = N-hydroxysuccinimidyl).

IT **221630-73-5P 221630-74-6P 224444-84-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(delivery of polyethylene glycol-conjugated mols. from degradable hydrogels)

IT **224444-79-5P 224444-89-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(delivery of polyethylene glycol-conjugated mols. from degradable hydrogels)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2003 ACS

| | |
|---|---|
| ACCESSION NUMBER: | 1999:242945 HCAPLUS |
| DOCUMENT NUMBER: | 131:72399 |
| TITLE: | Multivalent Thioether-**Peptide** **Conjugates**: B Cell Tolerance of an Anti-**Peptide** Immune Response |
| AUTHOR(S): | Jones, David S.; Coutts, Stephen M.; Gamino, Christina A.; Iverson, G. Michael; Linnik, Matthew D.; Randow, Martina E.; Ton-Nu, Huong-Thu; Victoria, Edward J. |
| CORPORATE SOURCE: | La Jolla Pharmaceutical Company, San Diego, CA, 92121, USA |
| SOURCE: | Bioconjugate Chemistry (1999), 10(3), 480-488 CODEN: BCCHES; ISSN: 1043-1802 |
| PUBLISHER: | American Chemical Society |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

AB Antibodies which bind .beta.2-glycoprotein I (.beta.2GPI) are assocd. with antiphospholipid syndrome. Synthetic **peptide** mimotopes have been discovered which compete with .beta.2GPI for binding to selected anti-.beta.2GPI. A thiol-contg. linker was attached to the N-terminus of two cyclic thioether **peptide** mimotopes, **peptides** 1a and 1b. The resulting **peptides**, with linker attached, were reacted with two different haloacetylated platforms to prep. four

tetravalent **peptide**-platform **conjugates** to be tested as B cell toleragens. The linker-contg. **peptides** were reacted with maleimide-derivatized keyhole limpet hemocyanin (KLH) to provide **peptide**-KLH **conjugates**. **Peptides** 1a and 1b were also modified by acylation with 3-(4'-hydroxyphenyl)propionic acid N-hydroxysuccinimidyl ester. The resulting hydroxyphenyl **peptides** were radioiodinated and used to measure anti-**peptide** antibody levels. The KLH **conjugates** were used to immunize mice to generate an anti-**peptide** immune response. The immunized mice were treated with the **conjugates** or saline soln. and boosted with the appropriate **peptide**-KLH **conjugate**. Three of the four **conjugates** suppressed the formation of anti-**peptide** antibody. The stabilities of the **conjugates** in mouse serum were measured, and the relative stabilities did not correlate with ability to suppress antibody formation.

IT **186698-35-1P 228403-74-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction of; multivalent thioether-**peptide** **conjugates** in relation to B-cell tolerance)

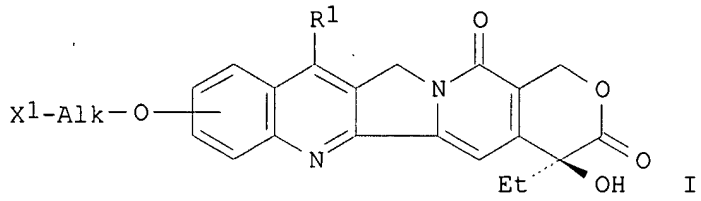
IT **134978-94-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of; multivalent thioether-**peptide** **conjugates** in relation to B-cell tolerance)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

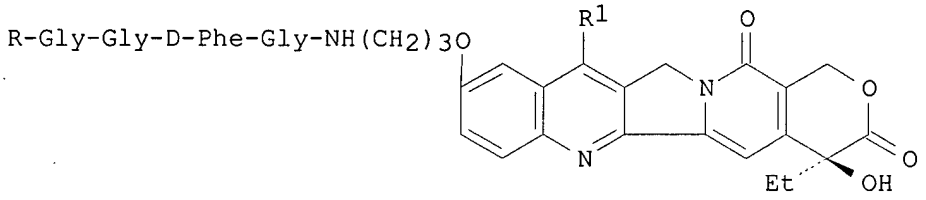
L15 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:665874 HCAPLUS
DOCUMENT NUMBER: 130:4084
TITLE: Preparation of polysaccharide-**peptide** or amino acid-linked camptothecin **conjugates** as antitumor agents
INVENTOR(S): Tsujihara, Kenji; Kawaguchi, Takayuki; Okuno, Akira; Yano, Toshiaki
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 44 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 10273488 | A2 | 19981013 | JP 1998-16763 | 19980129 |
| JP 3322203 | B2 | 20020909 | | |

PRIORITY APPLN. INFO.: JP 1997-17280 A 19970131
OTHER SOURCE(S): MARPAT 130:4084
GI



I



II

AB The title compds., which are camptothecin derives. [I; R1 = (un)substituted lower alkyl; X1 = NHR2, OH; wherein R2 = H, lower alkyl; Alk = linear or branched alkylene optionally interrupted by O] linked to carboxy-contg. polysaccharide through a peptide or amino acid, are prepd. These compds. are reduced in toxicity and markedly enhanced in antitumor potency. Claimed is a pharmaceutical compn. contg. I as the active ingredient for treatment of cancers of lung, uterus, ovary, breast, digestive organs (large intestine, stomach, or pancreas), liver, kidney, prostate gland, and neck, malignant lymphoma, and leukemia. Thus, N-peptidyl-10-(3-aminopropoxy)-(20S)-camptothecin deriv. (II; R = H) (prepn. given) was condensed with carboxymethyl dextran sodium salt using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride in H2O to give the title compd. II (R = carboxymethyl dextran sodium salt residue), which at 60 mg/kg (single dosage) in vivo inhibited 100% the proliferation of human breast cancer MX-1 cell in mice within 26 days after the drug administration.

IT **215592-09-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of polysaccharide-**peptide** or amino acid-linked camptothecin **conjugates** as antitumor agents)

IT **215592-10-2P 215592-11-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of polysaccharide-**peptide** or amino acid-linked camptothecin **conjugates** as antitumor agents)

L15 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:603738 HCAPLUS
DOCUMENT NUMBER: 129:302868
TITLE: Efficient Solid-Phase Synthesis of Peptide-Substituted Alkanethiols for the Preparation of Substrates That Support the Adhesion of Cells
AUTHOR(S): Houseman, Benjamin T.; Mrksich, Milan
CORPORATE SOURCE: Department of Chemistry, The University of Chicago,

Chicago, IL, 60637, USA
SOURCE: Journal of Organic Chemistry (1998), 63(21), 7552-7555
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors describe a rapid and efficient method, based on solid-phase **peptide** synthesis, for prepg. alkanethiols terminated with **peptide** ligands. This methodol. is utilized to synthesize a Gly-Arg-Gly-Asp-Ser alkanethiol **conjugate** and demonstrate that monolayers prepd. from this compd. support the adhesion and spreading of fibroblast cells.
IT **214626-69-4P 214626-70-7P 214626-71-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(efficient solid-phase synthesis of peptide-substituted alkanethiols for as cell adhesion substrates)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:141010 HCAPLUS
DOCUMENT NUMBER: 126:143310
TITLE: Immunoreactive **peptides, conjugates** and methods for treatment of antiphospholipid (aPL) antibody-mediated pathologies
INVENTOR(S): Victoria, Edward Jess; Marquis, David Matthew; Jones, David S.; Yu, Lin
PATENT ASSIGNEE(S): La Jolla Pharmaceutical Company, USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9640197 | A1 | 19961219 | WO 1996-US9976 | 19960606 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN | | | | |
| US 5874409 | A | 19990223 | US 1995-482651 | 19950607 |
| CA 2223687 | AA | 19961219 | CA 1996-2223687 | 19960606 |
| AU 9662710 | A1 | 19961230 | AU 1996-62710 | 19960606 |
| AU 711192 | B2 | 19991007 | | |
| EP 833648 | A1 | 19980408 | EP 1996-921498 | 19960606 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1192153 | A | 19980902 | CN 1996-196006 | 19960606 |
| JP 11507822 | T2 | 19990713 | JP 1996-502123 | 19960606 |
| CN 1225015 | A | 19990804 | CN 1997-196260 | 19970606 |

PRIORITY APPLN. INFO.: US 1995-482651 A 19950607
WO 1996-US9976 W 19960606
OTHER SOURCE(S): MARPAT 126:143310
AB APL analogs that bind specifically to B cells to which an aPL epitope

binds are disclosed. Optimized analogs lacking T cell epitope(s) are useful as conjugates for treating aPL antibody-mediated diseases. Methods of prepg. and identifying said analogs, methods of treatment using said analogs, methods and compns. for prepg. conjugates of said analogs and diagnostic immunoassays for aPL antibodies are disclosed.

IT **134978-94-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of antiphospholipid immunoreactive **peptide conjugates** for treatment of antiphospholipid antibody-mediated pathologies)

IT **118988-07-1P 186698-35-1P 186698-38-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of antiphospholipid immunoreactive **peptide conjugates** for treatment of antiphospholipid antibody-mediated pathologies)

L15 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:184037 HCAPLUS
DOCUMENT NUMBER: 124:254781
TITLE: Conjugates of metal complexes and oligoribonucleotides which bind specifically to selected target structures
INVENTOR(S): Dinkelborg, Ludger; Hilger, Christoph-Stephan; Niedballa, Ulrich; Platzek, Johannes; Raduechel, Bernd; Speck, Ulrich
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 25 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4424922 | A1 | 19960118 | DE 1994-4424922 | 19940714 |
| US 2002077306 | A1 | 20020620 | US 1995-488290 | 19950607 |
| IL 114237 | A1 | 20000831 | IL 1995-114237 | 19950620 |
| CA 2194558 | AA | 19960201 | CA 1995-2194558 | 19950630 |
| WO 9602274 | A1 | 19960201 | WO 1995-EP2539 | 19950630 |
| W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9529791 | A1 | 19960216 | AU 1995-29791 | 19950630 |
| EP 777498 | A1 | 19970611 | EP 1995-925792 | 19950630 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| CN 1152879 | A | 19970625 | CN 1995-194000 | 19950630 |
| HU 76329 | A2 | 19970828 | HU 1997-100 | 19950630 |
| JP 10503182 | T2 | 19980324 | JP 1995-504630 | 19950630 |
| RU 2165771 | C2 | 20010427 | RU 1997-102039 | 19950630 |
| ZA 9505895 | A | 19960219 | ZA 1995-5895 | 19950714 |
| NO 9700141 | A | 19970314 | NO 1997-141 | 19970113 |
| AU 9920360 | A1 | 19990617 | AU 1999-20360 | 19990312 |
| AU 721330 | B2 | 20000629 | | |

PRIORITY APPLN. INFO.:
DE 1994-4424922 A 19940714
US 1994-336127 B2 19941104
US 1994-336128 B2 19941104
DE 1994-4445078 A 19941205

| | | |
|---|---|---|
| US 1994-357573 | B2 | 19941215 |
| US 1994-358065 | B2 | 19941215 |
| US 1995-409813 | B1 | 19950324 |
| AU 1995-29791 | A3 | 19950630 |
| WO 1995-EP2539 | W | 19950630 |

AB Conjugates of modified oligonucleotides with complexes of radioactive or stable metal isotopes, which bind specifically to biol. target structures, are useful in diagnostic imaging and radiotherapy. The oligonucleotides are modified to render them resistant to degrdn. by endogenous nucleases, e.g. by O-alkylation, halogenation, amination, or redn. at the 2' position or by replacement of phosphodiester groups by phosphorothioate, phosphorodithioate, or alkylphosphonate linkages. The oligonucleotides are selected from a random mixt. for binding to a target such as a non-nucleic acid macromol., tissue, or organ. Thus, a 30-mer oligonucleotide ligand for NGF was conjugated with the linker .beta.-cyanoethyl N,N-diisopropylamino-6-(trifluoroacetamido)-1-hexylphosphoramidite, then with 10-[7-(4-isothiocyanatophenyl)-2-hydroxy-5-oxo-7-(carboxymethyl)-4-azaheptyl]-1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane (prepn. given), and complexed with 111In(III) for use as a radiodiagnostic agent.

IT **131274-04-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(**conjugates** of metal complexes and oligoribonucleotides which bind specifically to selected target structures)

L15 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:319762 HCAPLUS
DOCUMENT NUMBER: 122:89553
TITLE: PEG hydrazone and PEG oxime linkage forming reagents and protein derivatives.
INVENTOR(S): Wright, David E.
PATENT ASSIGNEE(S): Ortho Pharmaceutical Corp., USA
SOURCE: Eur. Pat. Appl., 47 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 605963 | A2 | 19940713 | EP 1993-309825 | 19931207 |
| EP 605963 | A3 | 19951108 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| CA 2110543 | AA | 19940610 | CA 1993-2110543 | 19931202 |
| FI 9305485 | A | 19940610 | FI 1993-5485 | 19931208 |
| NO 9304477 | A | 19940610 | NO 1993-4477 | 19931208 |
| ZA 9309214 | A | 19950608 | ZA 1993-9214 | 19931208 |
| AU 9352383 | A1 | 19940623 | AU 1993-52383 | 19931209 |
| JP 07196925 | A2 | 19950801 | JP 1993-340709 | 19931209 |

| | | |
|---|---|---|
| PRIORITY APPLN. INFO.: | US 1992-987739 | 19921209 |
| | US 1993-45052 | 19930407 |
| | US 1993-157343 | 19931123 |

AB Compds. for modifying polypeptides with PEG or other water-sol. org. polymers are described. The water-sol. polymer reagents include hydrazine, hydrazine carboxylate, semicarbazole, thiosemicarbazide, carbonic acid dihydrazide, carbazide, thiocarbazide, and arylhydrazide derivs. as well as oxylamine derivs. of water-sol. org. polymers, such as polyethylene glycol, polypropylene glycol, polyoxyethylated polyol,

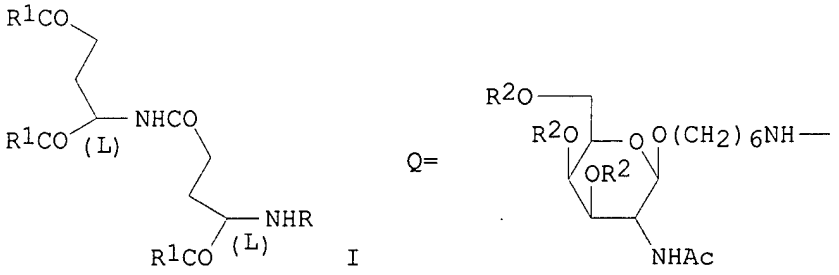
heparin, heparin fragments, dextran polysaccharides, polyamino acids, and polyvinyl alc. Kits for modifying polypeptides with the above water-sol. polymer reagents are also provided. Thus, erythropoietin was modified by oxidn. and treatment with monomethoxypolyoxyethylene semicarbazide and the product was sepd. by chromatog. The antigenicity and the effect on hematocrit levels of the above derivs. were demonstrated.

IT **160556-36-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and biol. activity of polyoxyethylene-coupled **protein** derivs.)

L15 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:164909 HCAPLUS
DOCUMENT NUMBER: 120:164909
TITLE: Preparation of glycosides and branched sugar **conjugates** with **peptides** or amino acids as pharmaceutical microparticle carriers
INVENTOR(S): Yamada, Harutami; Myoshi, Shiro; Azuma, Kunio; Nakabayashi, Akira; Yamauchi, Hitoshi; Watanabe, Hiroshi; Tanaka, Isao; Sasaki, Atsushi; Murahashi, Naoichi; Et, Al.
PATENT ASSIGNEE(S): Dei Dei Esu Kenkyusho Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 114 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 05202085 | A2 | 19930810 | JP 1992-232879 | 19920807 |

PRIORITY APPLN. INFO.: JP 1991-222214 19910807
GI




I

AB The title glycopeptides and glycosides (X1 - Xn+1)(AA)n [n = 0,1,2; when n = 0, (AA)n = single bond; when n =1, (AA)n = COCH2CH2(CO-)NH, COCH2(CO-)NH, COCH(CH2O-)NH; when n = 2, (AA)n = COCH2CH2CH(CO-)NHCOCH2CH2CH(CO-)NH, COCH2CH2CH(CO-)NHCOCH(CH2CH2CO-)NH, COCH2CH(CO-)NHCOCH2CH(CO-)NH, COCH2CH(CO-)NHCOCH(CH2CO-)NH, COCH2CH2CH(CO-)NHCOCH(CH2O-)NH, COCH2CH(CO-)NHCOCH(CH2O-)NH, COCH2CH(CO-)NHCOCH(CH2CH2CO-)NH, COCH2CH(CO-)NHCOCH2CH2CH(CO-)NH, COCH2CH2CH(CO-)NHCOCH(CH2CO-)NH, COCH2CH2CH(CO-)NHCOCH2CH(CO-)NH; X1 - Xn+1 = OR1 or NHR2 linked to the CO group of (AA)n, R linked to the oxy

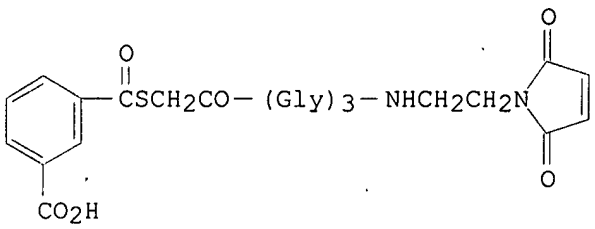
group of (AA)n; wherein R = (acetyl-protected) glycosyl group; R1 = H, alkali metal, C1-3 alkyl, CH2Ph; R2 = H, (CH2)aOR, (CH2CH2O)bR; a = 1-10; b = 1-8; some provisos given], useful as materials for liposomes for selectively delivering pharmaceuticals to organs, e.g. liver, and with improved microcirculation, are prepd. Thus, N-deprotection of galactosamine-contg. diglutamic acid deriv. (I; R = Me3CO2C, R1 = Q, R2 = Ac) (prepn. given) with CF3CO2H followed by amidation with HO2CCH2(OCH2CH2)3OC18H37 using DCC and N-hydroxysuccinimide in CH2Cl2 contg. Et3N gave I [R = C18H37(OCH2CH2)3OCH2CO, R1 = Q, R2 = Ac] which was O-deacetylated with NaOMe in MeOH to give I [R = C18H37(OCH2CH2)3OCH2CO, R1 = Q, R2 = H]. Liposomes contg. 3H-inulin were prepd. from L-palmitoylphosphtidylcholin, choresterol, dicetyl phosphate, and H3-inulin and administered to rats i.v. The liposomes rapidly disappeared from blood and were transfered to liver.

IT **153253-81-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of organ-selective liposome material)

L15 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:560829 HCAPLUS
DOCUMENT NUMBER: 119:160829
TITLE: One vial method for labeling **protein**/linker **conjugates** with technetium-99m
INVENTOR(S): Dean, Richard T.
PATENT ASSIGNEE(S): Centocor, USA
SOURCE: U.S., 20 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5180816 | A | 19930119 | US 1988-235908 | 19880824 |

PRIORITY APPLN. INFO.: US 1988-235908 19880824
OTHER SOURCE(S): MARPAT 119:160829
GI




I

AB A one-vial method for labeling **proteins** with radioisotopes Tc-99m, Re-186, Re-188, Re-189 and Re-191 is disclosed. The method comprises contacting in a single vial a mixt. of a reducing agent and a **protein** mol. covalently bound to sulfhydryl contg. bifunctional coupling agents RS(CH2)aCO(NHCHR3CO)f(OCH2CH2)cZ, RS(CH2)aCO(NHCHR3CO)f(OCH2CH2)cOCH2CO(OCH2CH2)cZ, or

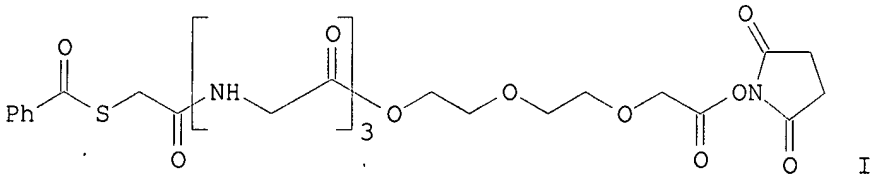
RS(CH2)aCO(NHCHR3CO)fOCH2CONHCH2CH2Z [a = 1-3; c = 1-7; f = 3-6; R = R1CO or R1S [R1 = (un)substituted alkyl or aryl]; R3 = H, (un)substituted alkyl or aryl; Z = ClCH2CONH, BrCH2CONH, ICH2CONH, N-substituted maleimido] with radioactive Tc or Re in an oxidized state. Thus, **peptide** deriv. I was prepd. and then coupled to antimyosin Fab'. The above **conjugate** was labeled with technetium-99m by treatment with sodium [Tc-99m]pertechnetate from a Mo-99/Tc-99m generator in the presence of glucarate and stannous ions.

IT **146551-11-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

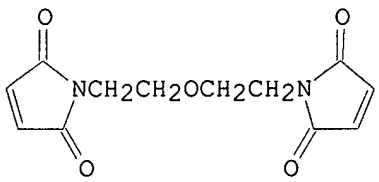
L15 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:534568 HCAPLUS
DOCUMENT NUMBER: 119:134568
TITLE: Crosslinking protein compositions having two or more identical binding sites for targeting therapy or diagnosis
INVENTOR(S): Dean, Richard T.; Lister-James, John; Boutin, Raymond H.
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5185433 | A | 19930209 | US 1990-506122 | 19900409 |

PRIORITY APPLN. INFO.: US 1990-506122 19900409
GI



I



II

AB The present invention provides crosslinked **protein** compns. consisting of .gtoreq.2 units of a target-specific **protein** (antibody) joined by binding SH groups on the target-specific **protein** units to a SH-selective crosslinking agent. These crosslinked **protein** compns. combine an increase in binding

affinity due to the presence of multiple identical binding sites and stability to reducing conditions. Therapeutic moieties or radiotracers may be attached to the crosslinked target-specific **protein** compn. for targeting therapy or radiodiagnosis. Thus, 99mTc-labeled crosslinked antiovarian cancer OC125 F(ab')2-I **conjugate** for radiodiagnosis was prepd. by (1) treating OC 125 F(ab')2 with II and iodoacetamide and (2) treating the crosslinked OC 125 F(ab')2 with I and then 99mTc glucarate.

IT **131274-04-9DP, conjugates** with antibodies and other substances **149299-81-0DP, conjugates** with antibodies and other substances
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, for targeting diagnosis or therapy)

L15 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:503320 HCAPLUS
DOCUMENT NUMBER: 119:103320
TITLE: **Proteins conjugates** with positively charged molecules with decreased blood clearance rates
INVENTOR(S): Dean, Richard T.; Boutin, Raymond H.; Lister-James, John
PATENT ASSIGNEE(S): Centocor, USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5162505 | A | 19921110 | US 1989-409150 | 19890919 |

PRIORITY APPLN. INFO.: US 1989-409150 19890919
OTHER SOURCE(S): MARPAT 119:103320

AB **Protein conjugates** comprising a **protein** covalently linked to .gtoreq.1 pos. charged mol., so that it has an overall net pos. charge in aq. conditions at physiol. pH, are disclosed. The pos. charged mol. comprise polymers of .gtoreq.3 subunits selected from the group consisting of amino acids contg. pos. charged side chains and alkylamines. The **protein conjugates** have decreased blood clearance rates compared to **conjugates** which do not have the pos. charged mol. The **protein conjugates** may further comprise diagnostic or therapeutic radionuclides bound to the **protein** or pos. charged mol. through bifunctional coupling agents. Penta-L-lysine-antimyosin Fab' **conjugate** (prepn. is given) was added to a soln. of succinimidyl benzothioacetylglycylglycinate and the modified **protein conjugate** was purified by Sephadex chromatog. The purified **protein conjugate** was deprotected and labeled with 99Tc. The deprotected and labeled **protein conjugate** was applied to a myosin-Sepharose column and bound and unbound fractions were counted and immunoreactivity detd. The immunoreactivity and recovery was 97, and 93% resp. The biodistribution of the **protein conjugate** was studied in mice.

IT **149299-81-0P**
RL: PRP (Properties); PREP (Preparation)
(prepn. and **conjugation** of, with **proteins**)

L15 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1993:148067 HCAPLUS
DOCUMENT NUMBER: 118:148067
TITLE: Preparation of bifunctional coupling agents as scintigraphic agents
INVENTOR(S): Dean, Richard T.; Boutin, Raymond H.; Weber, Robert W.
PATENT ASSIGNEE(S): Centocor, USA
SOURCE: U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 207,261.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5144043 | A | 19920901 | US 1988-235999 | 19880824 |
| US 5218128 | A | 19930608 | US 1988-207261 | 19880615 |

PRIORITY APPLN. INFO.: US 1988-207261 19880615
OTHER SOURCE(S): MARPAT 118:148067

AB The title coupling agents were prepd. for joining sulfhydryl-contg. **proteins** or **peptides** and metallic radionuclides. These agents contain a sulfhydryl-selective electrophile, a chelator contg. .gtoreq.1 protected thiol, and a linker. The title compds. are useful as immunodiagnostic and radiotherapeutic agents. Thus, PhCOSCH2CO(NHCH2CO)2NHCH2CO2H was esterified by Boc-NHCH2CH2OCH2CH2OH and the product was deprotected by CF3CO2H and then N-alkylated with BrCOCH2Br to give the PhCOSCH2CO(NHCH2CO)3O(CH2)O(CH2)2NHCOCH2Br (I) in 6% yield. I was **conjugated** with antifibrin antibody Fab' fragments, labeled with 99mTc, and the biodistribution of the labeled **conjugate** was detd.

IT **131274-04-9DP**, antifibrin Fab' and Tc-99m **conjugates**
**146551-07-7DP**, antifibrin Fab' and Tc-99m **conjugates**
**146551-09-9DP**, antifibrin Fab' and Tc-99m **conjugates**
**146551-11-3DP**, antifibrin Fab', antimyosin Fab' and Tc-99m **conjugates**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and biodistribution of)

IT **131274-04-9P 146551-07-7P 146551-09-9P 146551-11-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as bifunctional coupling agent for metallic radionuclide and sulfhydryl-contg. **protein** or **peptides**)

IT **146551-24-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for bifunctional coupling agents)

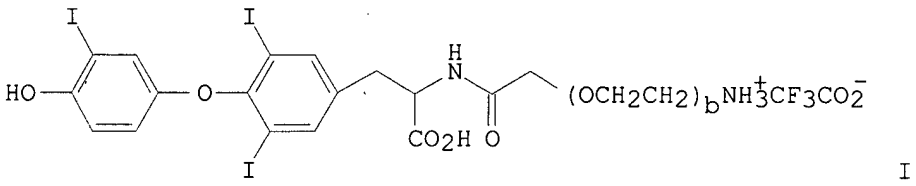
L15 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:152389 HCAPLUS
DOCUMENT NUMBER: 116:152389
TITLE: Preparation of improved marked haptens for immunoassay
INVENTOR(S): Kinkel, Tonio; Mayer, Andreas; Neuenhofer, Stephan; Oekonomopulos, Raymond
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4004296 | A1 | 19910814 | DE 1990-4004296 | 19900213 |
| EP 442372 | A1 | 19910821 | EP 1991-101656 | 19910207 |
| EP 442372 | B1 | 19950503 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL | | | | |
| AT 122149 | E | 19950515 | AT 1991-101656 | 19910207 |
| ES 2074179 | T3 | 19950901 | ES 1991-101656 | 19910207 |

PRIORITY APPLN. INFO.: DE 1990-4004296 19900213

GI



I

AB (XY)nZQm [X = biol. active substance (hapten); Y = COA(OCH2CH2)xNH, etc.; A = alkylene, CH2NHCO; x = 1-60; Z = protein, polypeptide; Q = chem. or phys. quantifiable labeling group; m, n = 1-4], useful in (chemiluminescent) immunoassay of haptens in liqs. (no details), were prepd. Thus, polyethylene glycol 600 was monochlorinated with SOCl2 in pyridine and the product was treated with N2CHCO2Et/BF3-Et2O, and then with NaN3 in DMF to give the monoazidomonocarboxylic acid deriv. This was hydrogenated in EtOH/CH2Cl2 over Pd/C followed by N-protection with triiodothyronine, and deprotection to give intermediate I (b .apprxeq. 7-19). This may be treated successively with poly(Glu:Lys 6:4)/ .gamma. -maleimidobutyric acid N-succinimidyl ester, S-acetylmercaptosuccinic anhydride, hydroxylamine hydrochloride, mercaptopropionic acid, and N-(4-methoxyphenyl)-N-[4-(2-succinimidyloxycarbonylethyl)benzenesulfonyl]-10-methylacridinium-9-carboxamide fluorosulfonate to give a title compd.

IT **139729-26-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for improved marked hapten)

L15 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:106333 HCAPLUS
DOCUMENT NUMBER: 116:106333
TITLE: Preparation of tetraazacycloalkane chelating agents and **conjugates** with **proteins**
INVENTOR(S): Dean, Richard T.; Weber, Robert W.
PATENT ASSIGNEE(S): Centocor, Inc., USA
SOURCE: U.S., 11 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5053503 | A | 19911001 | US 1989-312767 | 19890217 |

PRIORITY APPLN. INFO.: US 1989-312767 19890217
OTHER SOURCE(S): MARPAT 116:106333
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I and II; (E = group capable of reacting with a site on a **protein**; L = org. linking radical which may contain a cleavable site; R, R1 = H, alkyl; m, n, p, q = 2, 3; v, w = 0-2), and **conjugates** thereof, were prepd. Thus, 1,4,7,10-tetraazacyclododecane was converted to tetraalkylated title compd. III in several steps. III was stirred with antimyosin Fab' in DMF and the resulting **conjugate** was treated with 111InCl3 to give the radioactively labeled **conjugate**.

IT **139085-82-8DP**, reaction products with **proteins** and metal salts
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as drugs and diagnostics)

IT **139085-86-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for chelating agents-**protein conjugates**)

L15 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:38509 HCAPLUS
DOCUMENT NUMBER: 114:38509
TITLE: Enhanced kidney clearance with an ester-linked 99mTc-radiolabeled antibody Fab'-chelator conjugate
AUTHOR(S): Weber, Robert W.; Boutin, Raymond H.; Nedelman, Mark A.; Lister-James, John; Dean, Richard T.
CORPORATE SOURCE: Centocor, Inc., Malvern, PA, 19355, USA
SOURCE: Bioconjugate Chemistry (1990), 1(6), 431-7
CODEN: BCCHES; ISSN: 1043-1802
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Bifunctional chelators for labeling antibodies with 99mTc, based on the N3S core of mercaptoacetyltriglycine having ester or amide linking moieties, were synthesized and site-specifically attached to the sulfhydryl groups of the Fab' fragment of antimyosin. **Protein** labeling was quant. after 15 min; postlabeling purifn. was not necessary. The radiolabeled **conjugates** exhibited no loss of immunoreactivity. Under basic conditions, the ester-linked **conjugate** lost 95% of the radiolabel in the form of the 99mTc complex of mercaptoacetyltriglycine as detd. by reversed-phase HPLC, whereas the radioactivity in the amide-linked **conjugate** remained completely bound to the **protein**. In a mouse biodistribution study, the ester-linked **conjugate** showed a 2-fold enhancement in clearance from the kidney when compared to the amide-linked product.

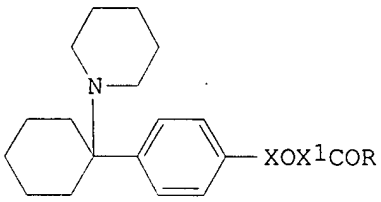
IT **131274-04-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and **conjugation** of, with technetium-99m and antibody F(ab')2 fragment)

L15 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:97667 HCAPLUS
DOCUMENT NUMBER: 96:97667

TITLE: Phencyclidine **conjugates** to antigenic **proteins** and enzymes
INVENTOR(S): Lin, Cheng I.; Singh, Prithipal
PATENT ASSIGNEE(S): Syva Co., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 4281065 | A | 19810728 | US 1979-6935 | 19790125 |

PRIORITY APPLN. INFO.: US 1979-6935 19790125
GI




I

AB Phencyclidine deriv. **conjugates** with antigenic **proteins** and enzymes I [X and X1 = alkylene, R = poly(amino acid)] are synthesized and employed for the prodn. of antibodies for use in immunoassays and enzyme immunoassays of phencyclidene, resp. Thus, 5-(4-(1-piperidinocyclohexan-1-yl)phenyl)-3-oxapentanoic acid [79849-45-9] was synthesized and **conjugated** with glucose 6-phosphate dehydrogenase [3867-15-0]. The resulting **conjugate** was sensitive to small changes in phencyclidine concns.

IT **79849-47-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and hydrolysis of)

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ENTER ANSWER SET OR SMARTSELECT L# OR (L15):end

=> select hit rn l15 1-30
E1 THROUGH E77 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 15:38:48 ON 10 APR 2003


Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 APR 2003 HIGHEST RN 502545-60-0
DICTIONARY FILE UPDATES: 9 APR 2003 HIGHEST RN 502545-60-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> fil hcaplu
FILE 'HCAPLUS' ENTERED AT 15:42:55 ON 10 APR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.


FILE COVERS 1907 - 10 Apr 2003 VOL 138 ISS 15
FILE LAST UPDATED: 9 Apr 2003 (20030409/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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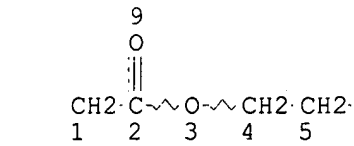
L1 STR

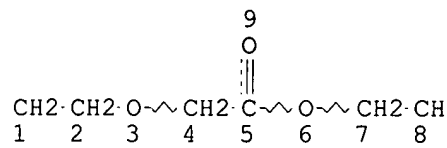



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L2 ( 6984)SEA FILE=REGISTRY SSS FUL L1
L3 ( 10066)SEA FILE=HCAPLUS L2

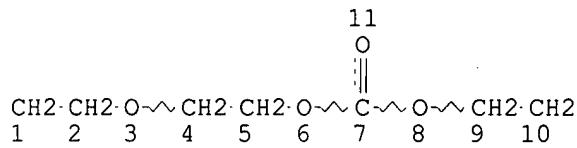
L4 89 SEA FILE=HCAPLUS L3 (L) (CONJUG? OR PROTEIN? OR ?PEPTIDE? OR ?INSULIN?)
L5 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 9

STEREO ATTRIBUTES: NONE
L6 813 SEA FILE=REGISTRY SSS FUL L5
L7 STR




NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE
L8 406 SEA FILE=REGISTRY SSS FUL L7
L9 570 SEA FILE=HCAPLUS L6
L10 360 SEA FILE=HCAPLUS L8
L12 6543 SEA FILE=REGISTRY INSULIN/BI
L13 155255 SEA FILE=HCAPLUS L12 OR INSULIN
L14 32181 SEA FILE=HCAPLUS CONJUG? (L)(PROTEIN? OR ?PEPTIDE? OR L13)
L15 30 SEA FILE=HCAPLUS L14 AND (L4 OR L9 OR L10)
L18 6990 SEA FILE=REGISTRY SSS FUL L1
L19 10071 SEA FILE=HCAPLUS L18
L20 30 SEA FILE=HCAPLUS L19 AND L14
L21 12 SEA FILE=HCAPLUS L20 NOT L15

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L21 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:221806 HCAPLUS
TITLE: Methods of synthesizing **insulin** **polypeptide**-oligomer **conjugates**, and proinsulin **polypeptide**-oligomer **conjugates** and methods of synthesizing same
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingham;

Ekwuribe, Nnochiri N.
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003022996 | A2 | 20030320 | WO 2002-US28428 | 20020906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-318197P P 20010907
US 2001-36744 A 20011221
US 2002-349462P P 20020118

AB Methods for synthesizing proinsulin **polypeptides** are described that include a contacting a proinsulin **polypeptide** including an **insulin polypeptide** coupled to one or more **peptides** by **peptide** bond(s) capable of being cleaved to yield the **insulin polypeptide** with an oligomer under conditions sufficient to couple the oligomer to the **insulin polypeptide** portion of the proinsulin **polypeptide** and provide a proinsulin **polypeptide**-oligomer **conjugate**, and cleaving the one or more **peptides** from the proinsulin **polypeptide**-oligomer **conjugate** to provide the **insulin polypeptide**-oligomer **conjugate**. Methods of synthesizing proinsulin **polypeptide**-oligomer **conjugates** are also described as are proinsulin **polypeptide**-oligomer **conjugates**. Methods of synthesizing C-**peptide polypeptide**-oligomer **conjugates** are also described.

IT **9004-10-8DP, Insulin, conjugates**
**9035-68-1DP**, Proinsulin, **conjugates**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesizing **insulin polypeptide**-oligomer **conjugates** and proinsulin **polypeptide**-oligomer **conjugates**)

IT **477775-76-1P 502487-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesizing **insulin polypeptide**-oligomer **conjugates** and proinsulin **polypeptide**-oligomer **conjugates**)

IT **59112-80-0D, c peptide, conjugates**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesizing **insulin polypeptide**-oligomer

Searched by M. Smith

**conjugates** and proinsulin **polypeptide**-oligomer **conjugates**)

L21 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:221462 HCAPLUS
TITLE: Pharmaceutical compositions of drug-oligomer conjugates for oral administration
INVENTOR(S): Soltero, Richard; Ekwuribe, Nnochiri N.; Opawale, Foyeke; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003022210 | A2 | 20030320 | WO 2002-US28536 | 20020906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-318193P P 20010907
US 2002-377865P P 20020503

AB An oral pharmaceutical compn. comprising a drug-oligomer **conjugate**, 0.1-15% of a fatty acid component, and 0.1-15% of a bile salt component is described. The drug, e.g., a **peptide** or **protein**, is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a wt.-to-wt. ratio of between 1:5 and 5:1. Methods of treating diseases in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. For example, tablets contg. an **insulin conjugate** HIM2 were prepd. by lyophilization of a mixt. contg. HIM2 2.5 g, Na cholate 30.0 g, oleic acid 10.0 g, 25% sucralose 8.0 g, flavor 4.0 g, capric acid 5.0 g, lauric acid 5.0 g, citric acid 67.2 g, trolamine 42.4 g, NaOH 18.8 g, pH adjusters (5N NaOH and 5N HCl) as needed, and water resulting in an amorphous powder. The powder (127.6 g) was blended with citric acid 29.7 g, sodium citrate 84.2 g, Tris base 106.7 g, microcryst. cellulose 24.8 g, and Explotab 9.4 g and compressed into tablets.

IT **11061-68-0D**, Human **insulin, conjugates** with methoxy(polyethylene glycol) hexanoic acid
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral compns. of drug-oligomer **conjugates** contg. bile salt and fatty acid)

IT **59112-80-0D**, C-**Peptide**, oligomer **conjugates**
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral compns. of drug-oligomer **conjugates** contg. bile salt and fatty acid)

IT **10108-28-8P 113395-48-5P 477775-74-9P 477775-75-0P 477775-76-1P 502487-23-2P 502487-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of oligomers for drug-oligomer conjugates for oral delivery)

L21 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:221460 HCAPLUS
TITLE: Pharmaceutical compositions of **insulin** drug-oligomer **conjugates**
INVENTOR(S): Soltero, Richard; Radhakrishnan, Balasingham; Ekwuribe, Nnochiri N.; Rehlaender, Bruce; Hickey, Anthony; Bovet, Li Li
PATENT ASSIGNEE(S): Nobex Corporation, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003022208 | A2 | 20030320 | WO 2002-US28429 | 20020906 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-318193P P 20010907
US 2002-377865P P 20020503

AB Pharmaceutical compns. that include an **insulin** drug-oligomer **conjugate**, a fatty acid component, and a bile salt component are described. The **insulin** drug is covalently coupled to an oligomeric moiety. The fatty acid component and the bile salt component are present in a wt.-to-wt. ratio of between 1:5 and 5:1. Methods of treating an **insulin** deficiency in a subject in need of such treatment using such pharmaceutical compns. are also provided, as are methods of providing such pharmaceutical compns. E.g., PEG derivs. of fatty acids such as hexanoic acid were prepd., activated and **conjugated** to **insulin** derivs.

IT **10108-28-8P 113395-48-5P 259228-98-3P 477775-74-9P 477775-75-0P 477775-76-1P 502487-23-2P 502487-24-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pharmaceutical compns. of **insulin** drug-oligomer **conjugates**)

IT **9004-10-8DP, Insulin, conjugates** with fatty acid-PEG derivs.

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. of **insulin** drug-oligomer **conjugates**)

L21 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:114145 HCAPLUS
DOCUMENT NUMBER: 138:149948
TITLE: Cell having modified cell membrane
INVENTOR(S): Nagamune, Teruyuki; Itoh, Chika; Yasukohchi, Tohru; Ohhashi, Syunsuke; Kubo, Kazuhiro
PATENT ASSIGNEE(S): NOF Corporation, Japan
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1283257 | A2 | 20030212 | EP 2002-17552 | 20020807 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
PRIORITY APPLN. INFO.: JP 2001-241843 A 20010809
AB A cell in which a reaction product of a substance to be modified and an amphipathic compd. is non-covalently bound to a cell membrane, wherein said compd. has the following features: (1) having one or more aliph. hydrocarbon groups at one end; (2) having one or more portions contg. a hydrophilic group in a mol.; and (3) having one or more reactive functional groups which are capable of covalently binding with the substance to be modified at an end different from the end in the above (1). Fluorescein-polyethylene oxide-modified dioleoylphosphatidylethanolamine was prepd. and stably anchored in mouse fibroblast NIH3T3 cell membranes.
IT **496050-85-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(cell having cell membrane modified by noncovalently bound reaction product of substance and amphipathic compd.)
IT **496050-86-3DP**, fluorescein derivs.
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(noncovalent binding to cell membrane; cell having cell membrane modified by noncovalently bound reaction product of substance and amphipathic compd.)

L21 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:757702 HCAPLUS
DOCUMENT NUMBER: 134:71479
TITLE: Synthesis and antiproliferative activity of unsaturated quinoline derivatives
AUTHOR(S): Montgomery, Gerard J.; McKeown, Paul; McGown, Alan T.; Robins, David J.
CORPORATE SOURCE: Department of Chemistry, University of Glasgow, Glasgow, G12 8QQ, UK
SOURCE: Anti-Cancer Drug Design (2000), 15(3), 171-181
CODEN: ACDDEA; ISSN: 0266-9536
PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:71479

AB Knoevenagel condensation of quinoline 6-, 7- and 8-carboxaldehyde with malononitrile derivs. was used to produce a series of 23 quinoline-tyrphostins. Some of these heteroarom. tyrphostins were potent inhibitors of the epidermal growth factor (EGF) receptor kinase and were moderately active against the MCF7 breast cancer cell line. The order of potency was 7- > 6- > 8-substituted quinoline, which indicates that increased activity of the 7-substituted quinolines is assocd. with electron deficiency at the 7-position in the quinoline ring. The most active compd., formed from 7-quinolinecarboxaldehyde and Et cyanoacetate, had an IC50 value of 2.3 .mu.M. The prepd. compds. showed similar IC50 values against the MCF7 and MCF7/ADR cell lines (the latter shows fourfold increased **protein** tyrosine kinase activity) except for the compds. formed from 6-quinolinecarboxaldehyde and malononitrile and 7-quinolinecarboxaldehyde and cyanoacetamide, which showed a significant (11- and 42-fold, resp.) increase in potency against the MCF7/ADR cell line. Furthermore, no assocn. was found between growth inhibition and inhibition of the EGFR **protein** tyrosine kinase (PTK), using a cell-free assay. In addn., new compds. were prepd. from 2- and 4-quinolinecarboxaldehyde with extended **conjugation** in the side chains or with methoxypolyethoxyethyl esters in the side chain to increase water soly. These compds. showed substantial cytotoxicity, with IC50 values in the range 1-25 .mu.M, but similar values were obsd. against both cell lines. No assocn. was found between inhibition of PTK and growth inhibition, again indicating that their mode of action may not be specific for the EGF receptor.

IT **315178-31-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and Knoevenagel condensation with quinolinecarboxaldehydes)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:471436 HCAPLUS
DOCUMENT NUMBER: 129:78811
TITLE: Receptor membranes.
INVENTOR(S): Cornell, Bruce Andrew; Braach-maksvytis, Vijolrta Lucija Brinislava
PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research Institute, Australia
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5766960 | A | 19980616 | US 1995-449895 | 19950523 |
| US 5436170 | A | 19950725 | US 1990-473932 | 19900125 |
| US 5693477 | A | 19971202 | US 1995-447569 | 19950523 |
| US 5741712 | A | 19980421 | US 1995-448178 | 19950523 |
| PRIORITY APPLN. INFO.: | | | AU 1987-3346 | 19870727 |
| | | | AU 1987-3348 | 19870727 |
| | | | AU 1987-3453 | 19870731 |

AU 1987-4478 19870921
US 1990-473932 19900125
WO 1988-AU273 19880727

AB A membrane comprising a closely packed array of self-assembling amphiphilic mols., and is characterized in that it incorporates a plurality of ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. **conjugated** with a supporting entity. The ion channel is selected from the group consisting of **peptides** capable of forming helixes and aggregates thereof, coronands, cryptands, podands and combinations thereof. In the amphiphilic mols. comprising a receptor mol. **conjugated** with a supporting entity, the receptor mol. has a receptor site and is selected from the group consisting of Igs, antibodies, antibody fragments, dyes, enzymes and lectins. "The supporting entity is selected from the group consisting of a lipid head group, a hydrocarbon chain(s), a cross-linkable mol. and a membrane **protein**. The supporting entity is attached to the receptor mol. at tan end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferable gated. Such membranes may be used in the formation of sensing devices.

IT **124804-88-2P 124804-89-3P 209266-70-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(receptor membranes)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:761698 HCAPLUS
DOCUMENT NUMBER: 126:33023
TITLE: Hybrid phthalocyanine derivatives and their uses
INVENTOR(S): Buechler, Kenneth F.; Noar, Joseph B.; Tadesse, Lema
PATENT ASSIGNEE(S): Biosite Diagnostics Incorporated, USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9629367 | A1 | 19960926 | WO 1996-US3833 | 19960322 |
| W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | |
| CA 2215727 | AA | 19960926 | CA 1996-2215727 | 19960322 |
| AU 9653188 | A1 | 19961008 | AU 1996-53188 | 19960322 |
| EP 820489 | A1 | 19980128 | EP 1996-909805 | 19960322 |
| EP 820489 | B1 | 20010711 | | |
| R: AT, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| JP 10508897 | T2 | 19980902 | JP 1996-528604 | 19960322 |
| AT 203045 | E | 20010715 | AT 1996-909805 | 19960322 |

PRIORITY APPLN. INFO.: US 1995-409825 A 19950323
WO 1996-US3833 W 19960322

AB Water-sol. hybrid phthalocyanine derivs., fluorescent latex particles incorporating which are useful in competitive and noncompetitive immunoassays and nucleic acid assays, have (1) .gtoreq.1 donor subunit

with a desired excitation peak and (2) .gtoreq.1 acceptor subunit with a desired emission peak, and are capable of intramol. energy transfer from the donor subunit to the acceptor subunit. They may also contain an electron-transfer subunit. Axial ligands may be covalently bound to the metals contained in the water-sol. hybrid phthalocyanine derivs. Ligands, ligand analogs, **polypeptides**, **proteins**, and nucleic acids can be linked to the axial ligands of the dyes to form **conjugates** useful in immunoassays and nucleic acid assays.

IT **183872-90-4P 183873-00-9P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(prepn. of water-sol. fluorescent hybrid phthalocyanine derivs. for immunoassays)

L21 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:630259 HCAPLUS
DOCUMENT NUMBER: 125:269871
TITLE: Polymer compositions and methods for directed ultrasound imaging
INVENTOR(S): Quay, Steven C.; Marrs, Christopher M.; Worah, Dilip M.
PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 727225 | A2 | 19960821 | EP 1996-630007 | 19960208 |
| EP 727225 | A3 | 19970115 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 08325165 | A2 | 19961210 | JP 1996-52387 | 19960214 |
| PRIORITY APPLN. INFO.: | | | US 1995-388468 | 19950214 |
| | | | US 1995-471568 | 19950606 |

AB Compns. for enhancing the ability to target gaseous microbubbles used in ultrasound contrast are described. The compns. include a cell adhesion mol. ligand which is incorporated into a desired mol. to form a conjugate. When the contrast agent is a colloidal dispersion, the conjugate is formed with a surfactant. When the agent is a solid microsphere, the conjugate is formed with a portion of the solid. Once the conjugate is formed, the surfactant or microsphere will adhere to the surface of desired target cells by coupling of the CAM ligand to cell adhesion mols. expressed on the cell surface. Thus, Jeffamine M-2070 was allowed to react with Sialyl Lewis X in the presence of NaCNBH3 and the product formed was uses in compns. and.

IT **182232-90-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymer compns. for directed ultrasound imaging)

L21 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:573281 HCAPLUS
DOCUMENT NUMBER: 121:173281
TITLE: Caged **Protein Conjugates** and Light-Directed Generation of **Protein** Activity: Preparation, Photoactivation, and Spectroscopic Characterization of Caged G-Actin

**Conjugates**
AUTHOR(S): Marriott, Gerard
CORPORATE SOURCE: Biomolecular and Cellular Dynamics Research Group, Max Planck Institute for Biochemistry, Martinsried bei Muenchen, 82152, Germany
SOURCE: Biochemistry (1994), 33(31), 9092-7
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple method is described to prep. caged (inactive) **protein** complexes using the amino group-directed photo-deprotection group [(nitroveratryl)oxy]chlorocarbamate (NVOC-Cl). This report describes how the polymn. activity of G-actin in physiol. salt soln. is lost upon **conjugation** of essential lysine residues of G-actin with NVOC-Cl. Reaction conditions were optimized to prep. caged G-actin in high yield, and the **conjugate** was characterized by biochem. and absorption spectroscopic methods. Upon excitation of caged G-actin in physiol. salt solns. with near-UV light, an efficient photo-deprotection reaction occurs via photoisomerization of the (nitrophenyl)ethylgroup of NVOC, which results in cleavage of the carbamate linkage between the protection reagent and G-actin. A std. irradn. condition was then defined which leads to photoactivation of F-actin from caged G-actin with a yield of more than 90%. Photoactivated F-actin was characterized according to its sedimentation behavior, electron microscopic anal., and sliding velocity on heavy meromyosin detd. with the in vitro motility assay. The results of these assays were similar to those obtained from unmodified F-actin. I also report the prepn. of caged G-actin **conjugated** at cysteine 374 with tetramethylrhodamine iodoacetamide and caged fluorescein maleimide. These caged G-actin **conjugates** can be used to generate fluorescent, polymn. competent G-actin following near-UV irradn. Given the widespread applications of caged substrates and ligands in cell biol., the simple method described herein to prep. and photoactivate caged **protein conjugates** is expected to advance investigations on the regulation of **protein** activity in living cells.

IT **250580-74-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(controlled drug release from, polymer blends in relation to)

L21 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:477743 HCAPLUS
DOCUMENT NUMBER: 121:77743
TITLE: Sensor membranes containing ionophores for ion selective electrodes and biosensors and their preparation and use in the detection of analytes
INVENTOR(S): Raguse, Burkhard; Cornell, Bruce Andrew; Braach-Maksvytis, Vijoleta Lucija Bronislava; Pace, Ronald John
PATENT ASSIGNEE(S): Australian Membrane and Biotechnology Research Institute, Australia; University of Sydney
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9407593 | A1 | 19940414 | WO 1993-AU509 | 19931001 |

Searched by M. Smith

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| EP 670751 | A1 | 19950913 | EP 1993-922449 | 19931001 |
| EP 670751 | B1 | 20011212 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 08505123 | T2 | 19960604 | JP 1993-508531 | 19931001 |
| AU 672638 | B2 | 19961010 | AU 1993-51444 | 19931001 |
| AU 9351444 | A1 | 19940426 | | |
| EP 1104883 | A2 | 20010606 | EP 2001-105279 | 19931001 |
| EP 1104883 | A3 | 20010718 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1106998 | A2 | 20010613 | EP 2001-105278 | 19931001 |
| EP 1106998 | A3 | 20010718 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1130386 | A1 | 20010905 | EP 2001-105275 | 19931001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1130387 | A1 | 20010905 | EP 2001-105276 | 19931001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| EP 1130388 | A1 | 20010905 | EP 2001-105277 | 19931001 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE | | | | |
| AT 210731 | E | 20011215 | AT 1993-922449 | 19931001 |
| ES 2169725 | T3 | 20020716 | ES 1993-922449 | 19931001 |
| US 5637201 | A | 19970610 | US 1995-406853 | 19950517 |
| US 5741409 | A | 19980421 | US 1997-833786 | 19970409 |
| US 5753093 | A | 19980519 | US 1997-833782 | 19970409 |
| US 5783054 | A | 19980721 | US 1997-826903 | 19970409 |
| US 5798030 | A | 19980825 | US 1997-826904 | 19970409 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| AU 1992-5069 | A | 19921001 |
| AU 1993-9863 | A | 19930708 |
| EP 1993-922449 | A3 | 19931001 |
| WO 1993-AU509 | W | 19931001 |
| US 1995-406853 | A3 | 19950517 |

AB The present invention relates to electrode membrane combinations for use in ion selective electrodes and biosensors. In addn., the present invention relates to methods for the prodn. of such electrode membrane combinations and the use of ion selective electrodes and biosensors incorporating such electrode membrane combinations in the detection of analytes. The present invention also relates to novel compds. used in the electrode membrane combinations. These novel compds. include a linker lipid for use in attaching a membrane including a plurality of ionophores to an electrode and providing a space between the membrane, the electrode being either in part or totally made up of the linker lipid. The linker lipid comprises within the same mol. a hydrophobic region capable of spanning the membrane, an attachment group used to attach the mol. to an electrode surface, a hydrophilic region between the hydrophobic region and the attachment group, and a polar head group region attached to the hydrophobic region at a site remote from the hydrophilic region. A Au on glass electrode was immersed in a soln. of 23-(20'-oxo-19'-oxaeicosa-(Z)-9'-ene)-70-phenyl-20,25,28,42,45-pentaoxo-24-aza-19,29,32,35,38,41,46,47,52,55-decaoxa-58,59-dithioahexaconta-(Z)-9-ene linker lipid and bis(2-hydroxyethyl)disulfide, the disulfide was allowed to adsorb, and the electrode was rinsed, dried, and clamped in a containment vessel. A soln. contg. glycerol monooleate, nonactin (ionophore), and tetradecane was added to the electrode, the electrode was rinsed with saline soln., and urease was nonspecifically bound to the lipid membrane surface. On the addn. of urea, the impedance of the

urease/ion selective electrode dropped more than that of the control (identical electrode lacking urease). Synthesis of membrane spanning lipids is described.

IT **156398-50-4 156398-51-5**
RL: ANST (Analytical study)
(in prepn. of linker lipid for attaching ionophore-contg. membrane to electrode)

IT **156370-83-1P 156370-84-2P 156370-85-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as membrane-spanning lipid for ionophores-contg. sensor membrane)

L21 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:115305 HCAPLUS
DOCUMENT NUMBER: 112:115305
TITLE: Receptor membranes for bisensor devices
INVENTOR(S): Cornell, Bruce Andrew; Braach-Maksvytis, Vijoleta Lucija Bronislava
PATENT ASSIGNEE(S): Commonwealth Scientific and Industrial Research Organization, Australia
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 8901159 | A1 | 19890209 | WO 1988-AU273 | 19880727 |
| W: AU, JP, US | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| AU 8821279 | A1 | 19890301 | AU 1988-21279 | 19880727 |
| AU 617687 | B2 | 19911205 | | |
| EP 382736 | A1 | 19900822 | EP 1988-907164 | 19880727 |
| EP 382736 | B1 | 19941102 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 03503209 | T2 | 19910718 | JP 1988-506329 | 19880727 |
| CA 1335879 | A1 | 19950613 | CA 1988-573217 | 19880727 |
| US 5436170 | A | 19950725 | US 1990-473932 | 19900125 |
| PRIORITY APPLN. INFO.: | | | AU 1987-3346 | 19870727 |
| | | | AU 1987-3348 | 19870727 |
| | | | AU 1987-3453 | 19870731 |
| | | | AU 1987-4478 | 19870921 |
| | | | WO 1988-AU273 | 19880727 |

AB A membrane comprising a closely packed array of self-assembling amphiphilic mols. is characterized in that it incorporates ion channels, and/or at least a proportion of the self-assembling mols. comprise a receptor mol. **conjugated** with a supporting entity. The ion channel is selected from **peptides** capable of forming helices and aggregates thereof, coronands, cryptands, podands, or combinations thereof. In the amphiphilic mols. comprising a receptor mol. **conjugated** with a supporting entity, the receptor mol. has a receptor site and is Igs, antibodies, antibody fragments, dyes, enzymes, or lectins. The supporting entity is a lipid head group, a hydrocarbon chain(s), a cross-linkable mol., or a membrane **protein**. The supporting entity is attached to the receptor mol. at an end remote from the receptor site. In preferred embodiments the ion channel is gramicidin A, and is preferably gated. Such membranes may be used in the formation

of sensing devices. A lipid gramicidin surface was prepd. on a Pd-coated glass electrode. The 1st monolayer contd. dodecanethiol:gramicidin (30:1) and the 2nd monolayer contd. 1-O-[11-(p-vinylphenoxy)undecanoyl]-2-O-octadecyl-3-O-acetoylglycerol (prepn. given): gramicidin R (prepd. by reacting gramicidin, 11-chloro-3,6,9-trioxaundec-1-yl succinate, dicyclohexyldiimide, and diethylaminopyridine) (100:1). The electrode was then incubated in an Fab soln. contg. Fab from 2 monoclonal antibodies to 2 distinct sites on human chorionic gonadotropin (hCG). HCG at 0.96 ng/mL in 0.1M NaCl gave an impedance of 106.20 .OMEGA. at 10 mHz corresponding to 4.8 .times. 104 conducting gramicidin channels, measured at 1 mHz. Before hCG, the impedance was 106.15 .OMEGA. at 10 mHz arising from 5.9 .times. 104 conducting gramicidin channels at 1 mHz.

IT **124804-88-2P 124804-89-3P 124804-90-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, in prepn. of receptor membrane for biosensor)

L21 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:453651 HCAPLUS
DOCUMENT NUMBER: 111:53651
TITLE: Diethylene glycol distearate as an embedding medium for immunofluorescence microscopy
AUTHOR(S): Valdimarsson, Gunnar; Huebner, Erwin
CORPORATE SOURCE: Dep. Zool., Univ. Manitoba, Winnipeg, MB, R3T 2T2, Can.
SOURCE: Biochemistry and Cell Biology (1989), 67(4-5), 242-5
CODEN: BCBIEQ; ISSN: 0829-8211
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Diethylene glycol distearate was tested for indirect immunofluorescence microscopy. Rhodnius ovarioles were embedded in diethylene glycol distearate, sectioned at 1-2 .mu.m, mounted onto coverslips, and stained with antitubulin antibodies followed by fluorescein-**conjugated** secondary antibodies. Flat, brightly stained sections with low background fluorescence were obtained routinely, suggesting that diethylene glycol diesterate may be generally applicable for immunofluorescence localization of cytoskeletal **proteins** in tissues.

IT **109-30-8**, Diethyleneglycol distearate
RL: ANST (Analytical study)
(embedding medium, for insect tissues for immunofluorescent staining)

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DR   321905-01-5
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24         RN   303096-30-2  REGISTRY
25         RN   262857-77-2  REGISTRY
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27         RN   259229-07-7  REGISTRY
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29         RN   259229-01-1  REGISTRY
30         RN   259228-98-3  REGISTRY
31         RN   250580-74-6  REGISTRY
DR   153190-96-6
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33         RN   229645-54-9  REGISTRY
34         RN   229645-52-7  REGISTRY
35         RN   229645-50-5  REGISTRY
36         RN   228403-74-5  REGISTRY
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38         RN   224444-84-2  REGISTRY
39         RN   224444-79-5  REGISTRY
40         RN   221630-74-6  REGISTRY
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41         RN   221630-73-5  REGISTRY
DR   224444-73-9
42         RN   215592-11-3  REGISTRY
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44         RN   215592-09-9  REGISTRY
45         RN   214626-71-8  REGISTRY
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47 RN **214626-69-4** REGISTRY
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51 RN **199869-48-2** REGISTRY
52 RN **186698-38-4** REGISTRY
53 RN **186698-35-1** REGISTRY
54 RN **183873-00-9** REGISTRY
55 RN **183872-90-4** REGISTRY
56 RN **182232-90-2** REGISTRY
57 RN **160556-36-5** REGISTRY
58 RN **156398-51-5** REGISTRY
59 RN **156398-50-4** REGISTRY
60 RN **156370-85-3** REGISTRY
61 RN **156370-84-2** REGISTRY
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63 RN **154773-34-9** REGISTRY
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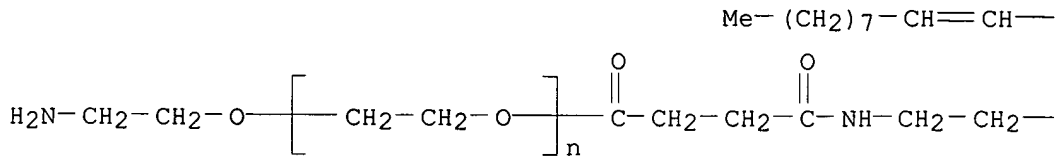
72 RN **139085-82-8** REGISTRY
73 RN **134978-94-2** REGISTRY
74 RN **131274-04-9** REGISTRY
75 RN **131029-43-1** REGISTRY
76 RN **124804-90-6** REGISTRY
77 RN **124804-89-3** REGISTRY
78 RN **124804-88-2** REGISTRY
79 RN **118988-07-1** REGISTRY
80 RN **113395-48-5** REGISTRY
81 RN **79849-47-1** REGISTRY
82 RN **70802-40-3** REGISTRY
83 RN **62304-85-2** REGISTRY
84 RN **28397-10-6** REGISTRY
85 RN **10233-14-4** REGISTRY
DR 240111-08-4
86 RN **10108-28-8** REGISTRY
87 RN **109-30-8** REGISTRY

=> d ide can 1 5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 87

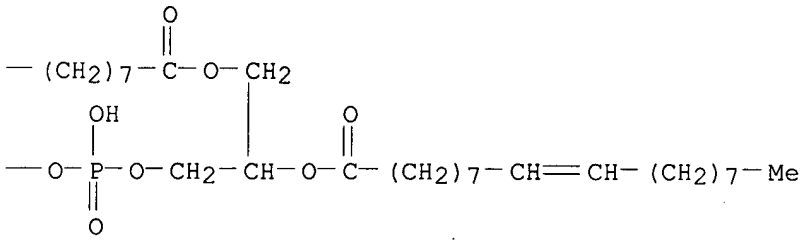
L23 ANSWER 1 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **496050-86-3** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-[(23Z)-9-hydroxy-9-oxido-1,4,15-trioxo-12-[[(9Z)-1-oxo-9-octadecenyl]oxy]-8,10,14-trioxa-5-aza-9-phosphadotriacont-23-en-1-yl]-.omega.-(2-aminoethoxy)- (9CI) (CA INDEX NAME)
MF (C2 H4 O)n C47 H87 N2 O11 P
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS

Searched by M. Smith

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

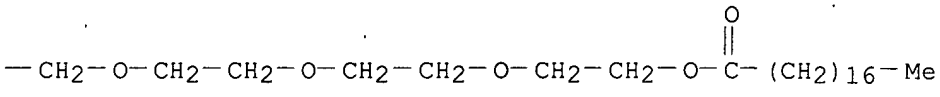
REFERENCE 1: 138:149948

L23 ANSWER 5 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **477775-74-9** REGISTRY
CN Octadecanoic acid, 25-phenyl-3,6,9,12,15,18,21,24-octaoxapentacos-1-yl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C41 H74 O10
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

PAGE 1-A



PAGE 1-B



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

Searched by M. Smith

4 REFERENCES IN FILE CA (1962 TO DATE)
6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:29120

REFERENCE 2: 138:16637

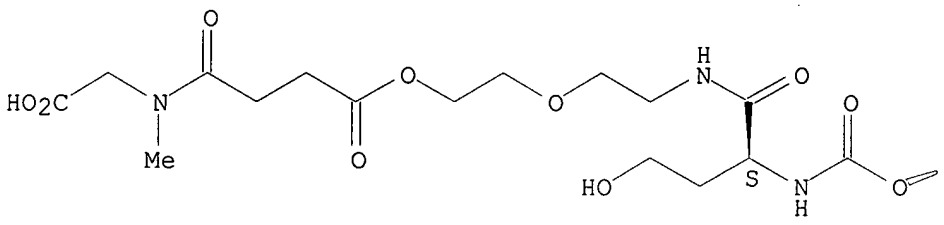
REFERENCE 3: 138:16636

REFERENCE 4: 138:16621

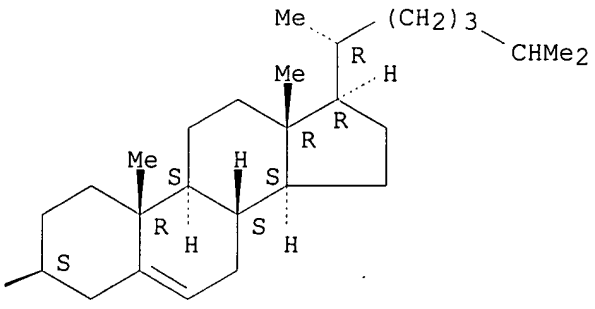
L23 ANSWER 10 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **352536-12-0** REGISTRY
CN Glycine, N-[[(3.beta.)-cholest-5-en-3-yloxy]carbonyl]-L-homoseryl-4-[2-(2-aminoethoxy)ethoxy]-4-oxobutanoyl-N-methyl- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C43 H71 N3 O10
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

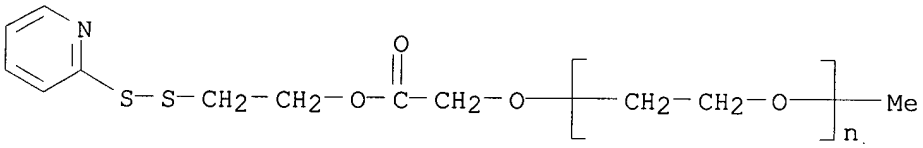
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

Searched by M. Smith

1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:167010

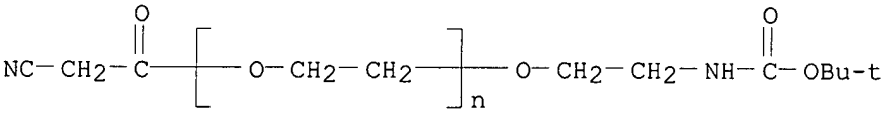
L23 ANSWER 15 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **331968-77-5** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-methyl-.omega.-[2-oxo-2-[2-(2-pyridinyldithio)ethoxy]ethoxy]- (9CI) (CA INDEX NAME)
MF (C2 H4 O)n C10 H13 N O3 S2
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS, USPAT2, USPATFULL



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:266736

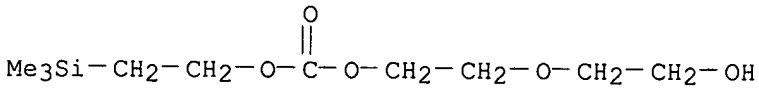
L23 ANSWER 20 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **321904-99-8** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-(cyanoacetyl)-.omega.-[2-[[(1,1-dimethylethoxy)carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)
DR 321905-01-5
MF (C2 H4 O)n C10 H16 N2 O4
CI PMS, COM
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:136545

L23 ANSWER 25 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **262857-77-2** REGISTRY
CN Carbonic acid, 2-(2-hydroxyethoxy)ethyl 2-(trimethylsilyl)ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C10 H22 O5 Si
SR CA
LC STN Files: CA, CAPLUS, CASREACT

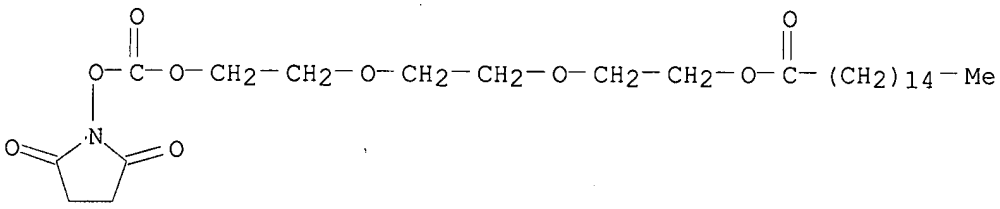


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:251326

L23 ANSWER 30 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **259228-98-3** REGISTRY
CN Hexadecanoic acid, 2-[2-[2-[[[(2,5-dioxo-1-pyrrolidinyl)oxy]carbonyl]oxy]ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C27 H47 N O9
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

5 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:29120

REFERENCE 2: 138:16637

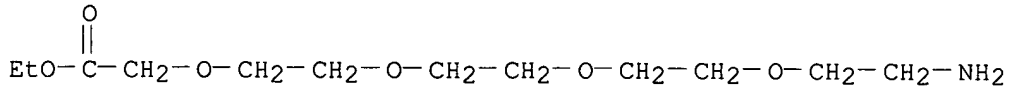
REFERENCE 3: 138:16636

REFERENCE 4: 138:16621

REFERENCE 5: 132:185416

L23 ANSWER 35 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **229645-50-5** REGISTRY
CN 3,6,9,12-Tetraoxatetradecanoic acid, 14-amino-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ethyl 14-amino-3,6,9,12-tetraoxatetradecanoate
FS 3D CONCORD
MF C12 H25 N O6
CI COM

SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

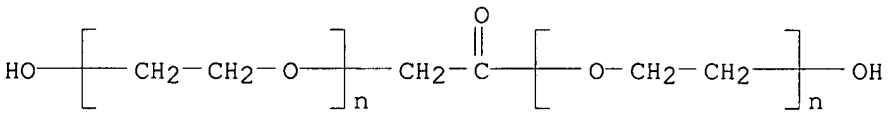
3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 132:313453

REFERENCE 2: 132:122950

REFERENCE 3: 131:88341

L23 ANSWER 40 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **221630-74-6** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.,.alpha.'-(1-oxo-1,2-ethanediyl)bis[.omega.-hydroxy- (9CI) (CA INDEX NAME)
DR 224444-75-1
MF (C2 H4 O)n (C2 H4 O)n C2 H4 O3
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



4 REFERENCES IN FILE CA (1962 TO DATE)
4 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:33720

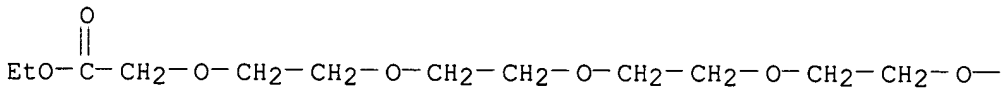
REFERENCE 2: 134:300865

REFERENCE 3: 130:357165

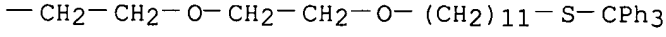
REFERENCE 4: 130:253129

L23 ANSWER 45 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **214626-71-8** REGISTRY
CN 14,17,20,23,26,29,32-Heptaoxa-2-thiatetratriacontan-34-oic acid, 1,1,1-triphenyl-, ethyl ester (9CI) (CA INDEX NAME)
MF C46 H68 O9 S
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



PAGE 1-B



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

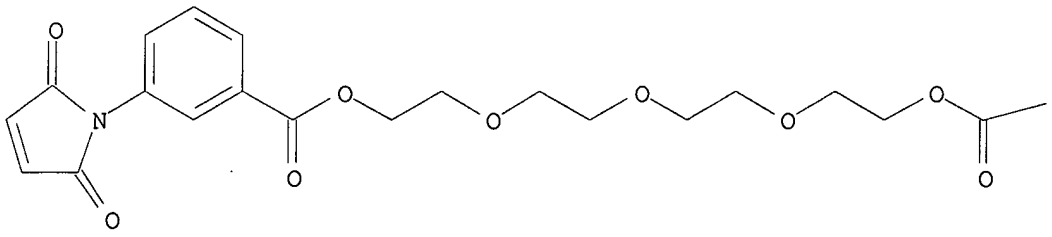
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 129:302868

L23 ANSWER 50 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **204652-44-8** REGISTRY
CN Cholest-5-en-3-ol (3.beta.)-, 13-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)phenyl]-13-oxo-3,6,9,12-tetraoxatridec-1-yl butanedioate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C50 H71 N O11
SR CA
LC STN Files: CA, CAPLUS

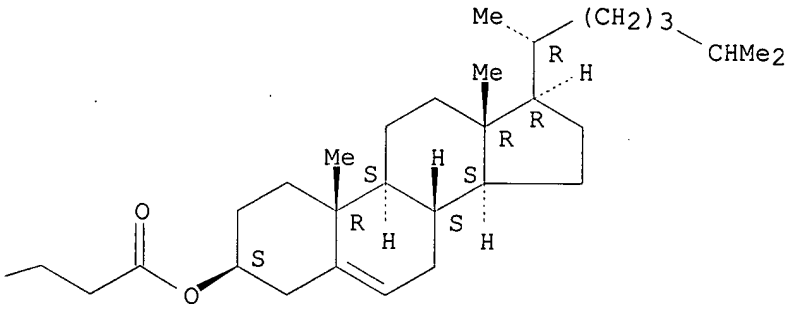
Absolute stereochemistry.

PAGE 1-A



Searched by M. Smith

PAGE 1-B




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

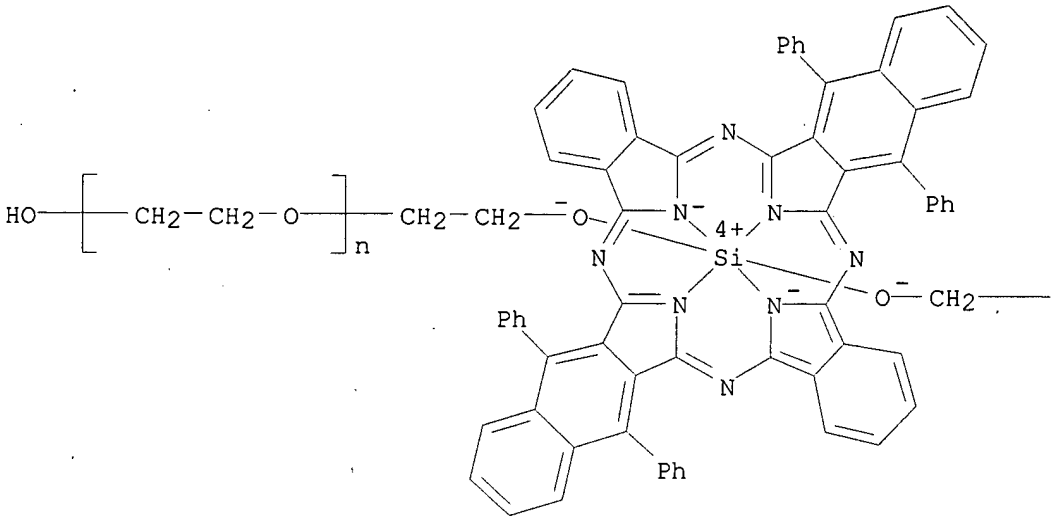
REFERENCE 1: 135:157549

REFERENCE 2: 133:168250

REFERENCE 3: 128:230562

L23 ANSWER 55 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **183872-90-4** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.OMEGA.-hydroxy-, ether with (OC-6-23)-bis(1,2-ethanediolato-.kappa.O)[8,13,24,29-tetraphenyl-33H,35H-dibenzo[b,l]dinaphtho[2,3-g:2',3'-q]porphyrazinato(2-)-.kappa.N33,.kappa.N34,.kappa.N35,.kappa.N36]silicon (2:1), mono[3-(acetylthio)propanoate] (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Poly(oxy-1,2-ethanediyl), .alpha.-hydro-.OMEGA.-hydroxy-, ether with (OC-6-23)-bis(1,2-ethanediolato-O)[8,13,24,29-tetraphenyl-33H,35H-dibenzo[b,l]dinaphtho[2,3-g:2',3'-q]porphyrazinato(2-)-N33,N34,N35,N36]silicon (2:1), mono[3-(acetylthio)propanoate]
MF (C2 H4 O)n (C2 H4 O)n C73 H52 N8 O6 S Si
CI CCS, PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



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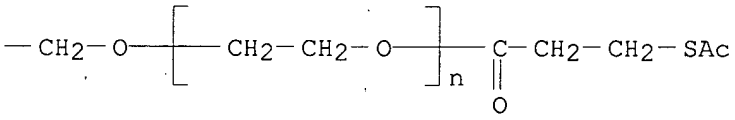


2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 135:78227

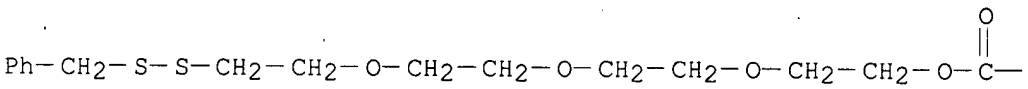
REFERENCE 2: 126:33023

L23 ANSWER 60 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **156370-85-3** REGISTRY
CN 5,8,11,14,17-Pentaoxaheneicosanedioic acid, 4,18-dioxo-, 3-[[16-[4-[[43-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-22,25,32,39-tetraoxo-19-[(3,7,11,15-tetramethylhexadecyl)oxy]-17,21-dioxa-24,31,38-triazatritetracont-1-yl]oxy]phenoxy]hexadecyl]oxy]-2-[(3,7,11,15-tetramethylhexadecyl)oxy]propyl 14-phenyl-3,6,9-trioxa-12,13-dithiatetradec-1-yl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

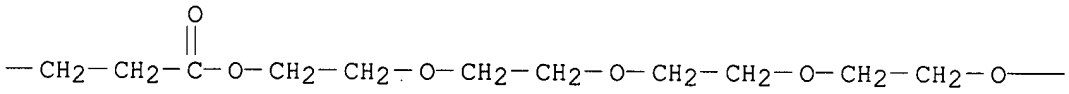
Searched by M. Smith

CN 1H-Thieno[3,4-d]imidazole, 5,8,11,14,17-pentaoxaheneicosanedioic acid deriv.
FS 3D CONCORD
MF C139 H247 N5 O26 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



PAGE 1-B



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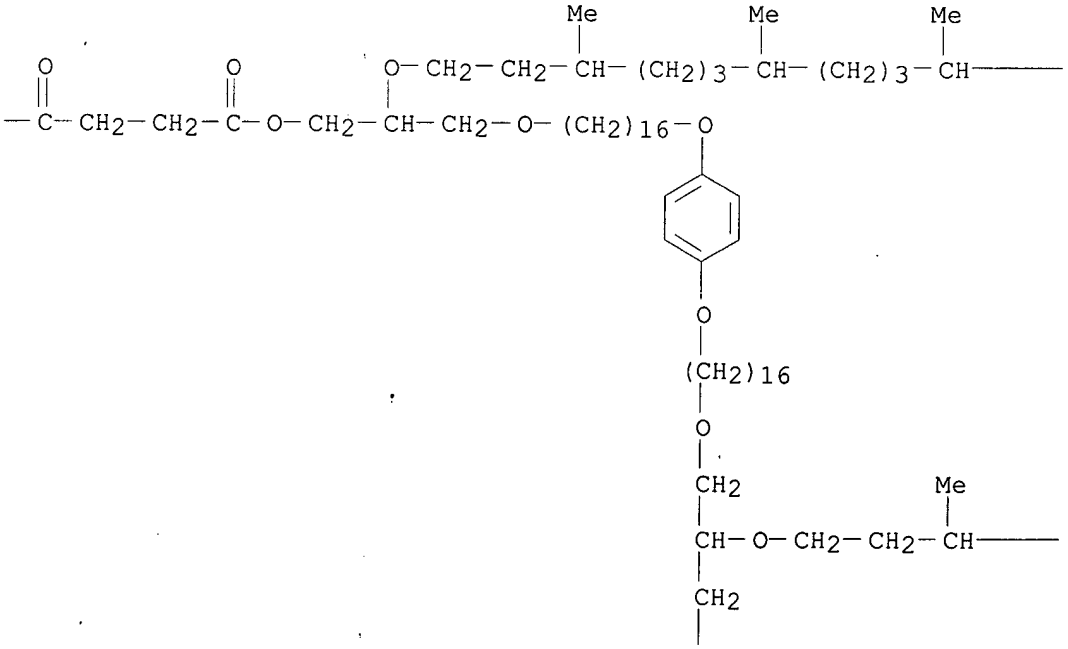
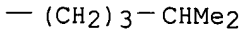
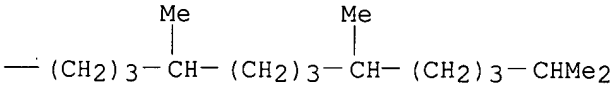


Searched by M. Smith

PAGE 1-D





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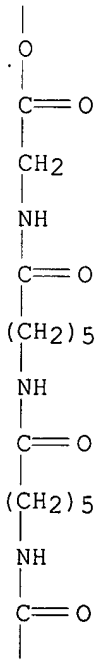
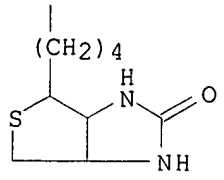


PAGE 3-C



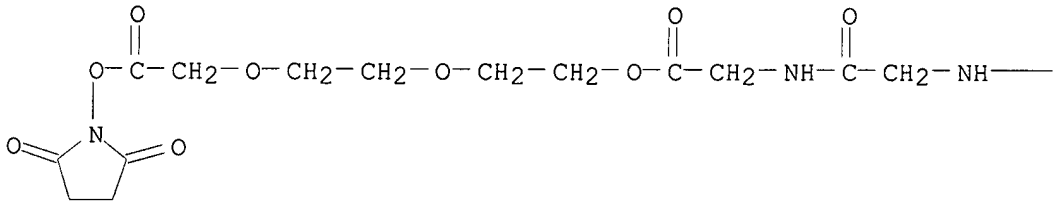
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 121:77743

L23 ANSWER 65 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **149299-81-0** REGISTRY
CN Glycine, N-[N-[N-[(benzoylthio)acetyl]glycyl]glycyl]-, 2-[2-[2-[(2,5-dioxo-1-pyrrolidinyl)oxy]-2-oxoethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)
MF C25 H30 N4 O12 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

PAGE 1-A



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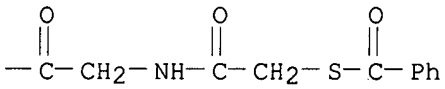


**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

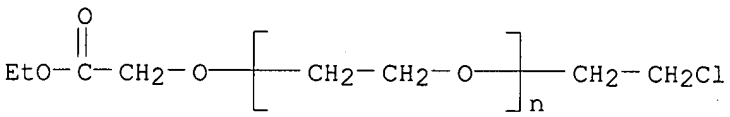
2 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 119:134568

REFERENCE 2: 119:103320

L23 ANSWER 70 OF 87 REGISTRY COPYRIGHT 2003 ACS

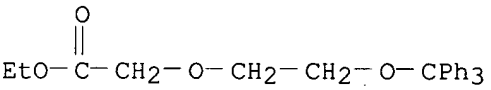
RN **139729-26-3** REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-(2-chloroethyl)-.omega.-(2-ethoxy-2-oxoethoxy)- (9CI) (CA INDEX NAME)
MF (C2 H4 O)n C6 H11 Cl O3
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 116:152389

L23 ANSWER 75 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **131029-43-1** REGISTRY
CN Acetic acid, [2-(triphenylmethoxy)ethoxy]-, ethyl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Ethyl [2-(triphenylmethoxy)ethoxy]acetate
MF C25 H26 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

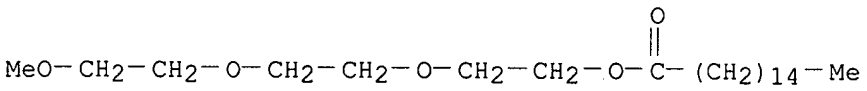
3 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 131:272145

REFERENCE 2: 127:121636

REFERENCE 3: 114:23805

L23 ANSWER 80 OF 87 REGISTRY COPYRIGHT 2003 ACS
RN **113395-48-5** REGISTRY
CN Hexadecanoic acid, 2-[2-(2-methoxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H46 O5
SR CA
LC STN Files: CA, CAPLUS



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1962 TO DATE)
3 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 108:114393

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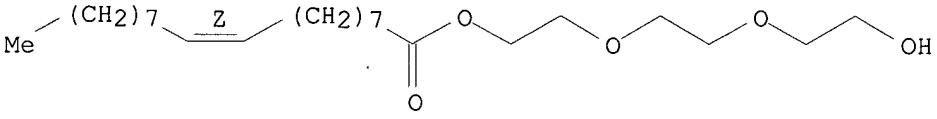
RN **10233-14-4** REGISTRY
CN 9-Octadecenoic acid (9Z)-, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 9-Octadecenoic acid (Z)-, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester
CN Oleic acid, 2-[2-(2-hydroxyethoxy)ethoxy]ethyl ester (8CI)
CN Triethylene glycol, monooleate
OTHER NAMES:
CN Motricol
CN Triethylene glycol oleate
FS STEREOSEARCH
DR 240111-08-4
MF C24 H46 O5
LC STN Files: CA, CAPLUS, CHEMCATS, CHEMLIST, TOXCENTER, USPATFULL
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Double bond geometry as shown.



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

6 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
6 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 134:76386

REFERENCE 2: 119:228494

REFERENCE 3: 96:87439

REFERENCE 4: 96:57579

REFERENCE 5: 81:96326

REFERENCE 6: 79:94338

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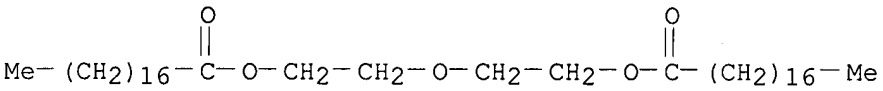
RN **109-30-8** REGISTRY
CN Octadecanoic acid, oxydi-2,1-ethanediyl ester (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Diethylene glycol, distearate (8CI)
CN Stearic acid, oxydiethylene ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN Oxydiethylene stearate
CN Witconol CAD
FS 3D CONCORD
MF C40 H78 O5
CI COM
LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, CHEMLIST, CSCHEM, HODOC*, IFICDB, IFIPAT, IFIUDB, MEDLINE, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

43 REFERENCES IN FILE CA (1962 TO DATE)
43 REFERENCES IN FILE CAPLUS (1962 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:314759

REFERENCE 2: 131:279317

REFERENCE 3: 129:335477

REFERENCE 4: 129:130325

REFERENCE 5: 129:75411

REFERENCE 6: 128:330159

REFERENCE 7: 128:53045

REFERENCE 8: 124:346616

REFERENCE 9: 124:185402

REFERENCE 10: 121:249934